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Health Effects Research Laboratory
Cincinnati, Ohio 45268

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VII. LEAD

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Cincinnati, Ohio 45219

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This document is a review of the scientific literature on the biological and environmental effects of lead. Included in the review are a general summary and a comprehensive discussion of the following topics as related to lead and specific lead compounds: physical and chemical properties; occurrence; synthesis and use; analytical methodology; biological aspects in microorganisms, plants, wild and domestic animals, and humans; distribution mobility, and persistence in the environment; and an assessment of present and potential health and environmental hazards, including lead in packaged foods. More than 950 references are cited. The document also contains an evaluation of potential hazard resulting from lead contamination in the environment and suggests current research needs.

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VII. LEAD

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FOREWORD

A vast amount of published material is accumulating as numerous research investigations are conducted to develop a data base on the adverse effects of environmental pollution. As this information is amassed, it becomes continually more critical to focus on pertinent, well-designed studies. Research data must be summarized and interpreted in order to adequately evaluate the potential hazards of these substances to ecosystems and ultimately to public health. The Reviews of the Environmental Effects of Pollutants (REEPs) series represents an extensive compilation of relevant research and forms an up-to-date compendium of the environmental effect data on selected pollutants.

Reviews of the Environmental Effects of Pollutants: VII. Lead, includes information on chemical and physical properties; pertinent analytical techniques; transport processes to the environment and subsequent distribution and deposition; impact on microorganisms, plants, and wildlife; toxicologic data in experimental animals including metabolism, toxicity, mutagenicity, teratogenicity, and carcinogenicity; and an assessment of health effects in man. The large volume of factual information presented in this document is summarized and interpreted in the initial chapter, "General Summary/Environmental Assessment" which presents an overall evaluation of the potential hazard resulting from present concentrations of lead in the environment. This overview chapter represents a major contribution by Dr. Paul Hammond of the University of Cincinnati, Dept. of Environmental Health. As a recognized authority in the field, Dr. Hammond's professional interpretation and synthesis of the literature gives great insight into past work and projected research trends.

The REEPs are intended to serve various technical and administrative personnel within the Agency in the decision-making processes, i.e. in the development of criteria documents and environmental standards, and for other regulatory actions. The breadth of these documents makes them a useful resource for public health personnel, environmental specialists, and control officers. Upon request these documents will be made available to any interested individuals or firms, both in and out of the government. Depending on the supply, the document can be obtained directly by writing to:

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PREFACE

Metallic lead was one of the earliest metals used by man. Since lead is now the most widely used heavy metal, and since lead poisoning has plagued mankind since antiquity, an enormous body of literature has developed on the biological aspects of lead. Thus, the principal problem in preparing this monograph was not in identifying and acquiring sufficient information to adequately encompass the topic, but assembling and coordinating what became a seemingly endless supply of pertinent and germane references. The wealth of candidate material for inclusion in this document which was deemed too significant to omit has resulted in a sizeable report.

In spite of the fact that lead has been studied so intensively for so long, comprehensive reviews of the literature frequently disclose areas warranting further investigation, and this review is no exception. For example, it would appear that the area of subclinical effects in children is one deserving further examination. The neurotoxic effects of lead include permanent damage to the central nervous system which may result in mental retardation, hyperactivity syndrome, psychological impairment, and deficiency in fine motor, adaptive, and language functions. The subclinical effects of lead upon adults including the aged also have not been resolved.

Interest in lead has not abated, and important new literature continues to appear. Also, as new and pending regulations governing the utilization and handling of lead begin to show measurable results, its environmental effects will begin to be altered from those described in this report, possibly shifting towards more subtle health effects. Their evaluation will pose challenging problems in designing and executing the requisite research studies.

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ABSTRACT

Lead, one of the oldest metals known to man, has by far the largest usage in the U.S. of any of the heavy metals, approaching 1.5 million metric tons per year. The largest use, for gasoline antiknock additives, results in the annual dispersion to the atmosphere of between 150,000 and 200,000 tons. Lead concentrations in the environment have increased significantly since the industrial revolution. Lead contamination reaching the environment is more or less immobilized in insoluble forms, e.g., as oxides, carbonates, or phosphates. Lead is not biomagnified to any significant extent in man's food chain. The transfer of lead to foods is minimized by its low solubility in environmental media, and by the ability of soil to bind lead ions. Although lead poisoning of animals does occur occasionally, the contribution of animal products to human lead burdens is negligible.

In earlier years acute lead poisoning was a common occupational problem in the metals and pigments industries, and in the manufacture of antiknock additives. Advances in industrial hygiene have virtually eliminated this problem; the few remaining problems are now being seriously addressed by new legislation.

The most serious toxicological problem at present appears to be lead poisoning in children, primarily as a result of pica and lead-based paints used on old homes. Legislation prompted by community action, mass screening, and improved therapy provide assurance that plumbism attributable to paint sources will continue to decline and possibly be eventually eradicated.

In recent years, adverse effects of lead have manifested themselves, especially in children, as minor neurological dysfunctions and impairments of motor and mental abilities. The overall impact of these effects has not been resolved.

Diet is the principal source of lead under normal circumstances; lead from air is a minor contributor. While lead is detectable in all foods, concentrations in food in cans with soldered side seams may exceed twice those in the raw food before canning.

This study reviews the environmental impact of lead. It includes a discussion of the physical and chemical properties, analytical methods, the biological aspects in microorganisms, plants, animals, and humans, environmental distribution and transformation and environmental interactions and their consequences.

This report was submitted in fulfillment of Contract Nos. 68-01-1837 and 68-03-2608 by Battelle Memorial Institute under the sponsorship of the U.S. Environmental Protection Agency. This report covers the period May 27, 1975 to February 28, 1978, and work was completed as of March 15, 1978.

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1.0 GENERAL SUMMARY/ENVIRONMENTAL ASSESSMENT

(Dr. Paul B. Hammond)

1.1 INTRODUCTION

This document is only one of several recent ones which have summarized portions of the vast literature dealing with the impact of lead on human health and the environment. Each has had a somewhat different purpose and focus. Thus, Lead in the Environment (NSF/RA-770214) is basically a summary of work conducted under the sponsorship of the National Science Foundation RANN program. It focuses mainly on the characteristics and transport of lead through the environment and on monitoring methodology. Air Quality Criteria for Lead (EPA 600/8-77-017, December, 1977) on the other hand, is basically a resource document intended for use in promulgating an air lead standard. As such, it omits a review of the literature dealing with effects of lead on bacteria, plants, domestic animals and wildlife. Similarly, the World Health Organization's recent publication, Environmental Health Criteria 3-Lead, is also concerned with critical evaluation of the literature dealing with the impact of lead on human health only. The present document most closely resembles "Airborne Lead in Perspective (NAS-NRC, 1972) as to breadth of coverage. Indeed, it may be considered a direct descendant of that earlier document not only as to the ground covered, but also as to the sponsorship by the Environmental Protection Agency.

This introductory chapter provides a general summary of the more detailed coverage provided in the subsequent chapters. In addition to this, it will attempt an assessment of the current problems begging resolution. This assessment expresses the views of specific contributors in behalf of a single agency. No claim to omniscience is implied. If this document, and particularly this chapter, triggers some controversy and debate in the scientific community, the effort and expenditures involved will have been justified. The worst that can happen is that no one will read it. This seems rather unlikely. We find today that lead is an issue which sparks debate and even class action suits by public interest groups, the economic and social impacts of which are likely to be considerable.

In the interest of organization, the topics considered in the separate chapters will be reviewed and commented upon in the order in which they appear in the document.

1.2 PHYSICAL AND CHEMICAL PROPERTIES AND ANALYSIS

There would probably be no great concern regarding lead today were it not for the fact that it has certain useful properties which have prompted its mining, smelting, and conversion to items of commerce.

Lead's high density, softness and relatively low melting point enable easy forming and casting. It has good resistance to oxidation and is fairly resistant to both alkaline and acid solutions. It and its alloys are readily cast, spun, stamped, rolled, extruded, and drawn. It can be readily bonded to other metals by various means. For all these reasons, it is used extensively in the metallic form.

The inorganic compounds of lead are moderately to highly insoluble. As a consequence, lead does not transfer readily from one phase in the environment to another, e.g., from rocks to water or from water to plants.

The organolead compounds in which lead is bound directly to one or more carbon atoms have unique properties. They are volatile, lipid-soluble and stable to most environmental conditions, susceptibility to photoxidation excepted. Tetraethyllead and tetramethyllead are the most common compounds of this class. Although they may occur in nature, the major known source is synthesis by man for use as a gasoline additive.

The analysis for lead presents numerous problems ranging from losses during sample storage and digestion to imprecisions during analysis resulting from matrix effects, non-specificity of method and incomplete atomization as in flameless atomic absorption methods. For most purposes, it appears that accuracy and precision are more serious problems than sensitivity. This is particularly evident in the case of analysis for lead in blood and urine. Interlaboratory comparison programs have revealed that highly discrepant results are common. The colorimetric dithizone method which was first developed more than forty years ago, is still considered reliable for most purposes when used by experienced analysts. Atomic absorption spectroscopy and anodic stripping voltammetry have largely displaced the colorimetric dithizone method. When used by experienced analysts, these methods are more specific and sensitive than are dithizone methods.

It seems clear that the current need is not so much for new methods as it is for more effective use of current methods. Concerns about the environmental impact of lead ultimately come down to a matter of relating effects to amounts or concentrations of lead in environmental and biological media. Assessments of risk are clearly dependent on reliable analytical data. Investigators should participate in interlaboratory comparison programs and should report in their scientific publications the accuracy and precision of their analytical methodology. There also is need for sensitive methodology which would identify the chemical form in which lead is found in various environmental media. This is necessary for studies involving the tracing of lead to sources of pollution, and for assessing the modes or mechanisms of lead impact in various systems. In order for such analytical methods to be useful, various separation and concentration methods must also be developed as appropriate for the particular problem at hand.

1.3 EFFECTS ON MICROORGANISMS

So far as bacteria and viruses are concerned, there is only very limited literature as to effects of lead and the possible significance thereof. As a matter of fact, there are no reports regarding lead interactions with viruses. Various species of bacteria are capable of converting trimethyllead to tetramethyllead. It is also possible that bacteria can convert inorganic lead to tetramethyllead, although this remains to be demonstrated.

At relatively high concentrations (10^{-4}M lead acetate) lead inhibits the incorporation of ^{14}C-leucine into E. coli t-RNA and thereby suggests that lead might inhibit protein synthesis. However, it should be noted that concentrations of lead approaching solubility limits have no detectable effect on growth rate and cell viability in two species of bacteria which have been studied. It appears from the limited studies reported to date that bacteria are relatively resistant to lead.

No high priority research needs are evident at this time in regard to interactions of lead with microorganisms. This may be because the research reported to date has focused too narrowly on individual species of microorganisms rather than on total integrated microbial communities It is possible that small effects on one or a few species in the world of microcrobes have cooperative effects which we have simply failed to perceive.

1.4 EFFECTS ON PLANTS

Consideration of the impact of lead on plant life falls into two general areas of concern. On the one hand, there is a concern for possible detrimental effects of lead on plants, either for economic reasons, as with food crops, or for esthetic reasons, i.e., concern for the varied plant life which is part of man's natural environment. There also exists the possibility that plants can serve as a biomagnification mechanism for the concentration and transfer of lead from soil and water to animal life, including man himself. Research studies to date strongly suggest that there is little cause for concern on either score. This is not to say that plants are totally resistant to detrimental lead effects. Nor is it to say that plants cannot under special circumstances serve as a medium for the transfer of toxic amounts of lead to animals and man. As a matter of fact, plant and animal foods constitute the major source of lead for the general population.

The National Academy of Sciences review, Airborne Lead in Perspective (1972), considered a relatively large volume of research on lead uptake, translocation, and effect in plants; it also pointed to research gaps (such as the uptake of aerial particulate deposited Pb and the need for root uptake studies of lead from naturally occurring soils). Over the ensuing years some of the questions asked by the 1972 report have been answered, but in other instances problems of lead-environmental interactions have proven to be even more complicated and elusive than had previously been thought. The most substantial conclusion to arise from these studies is that it is impossible to extrapolate effects of lead on plants grown under one set of environmental conditions to other situations without the very careful consideration of soil and plant factors affecting lead availability.

In most instances the source of lead with potential effects on plants has been from aerosols. Since most such particles are relatively large, their deposition is highly localized; i.e., within several hundred meters of roadways in the case of lead emitted from auto exhausts. Lead from aerosol sources is deposited on leaf surfaces and also comes in contact with roots as a result of soil contamination. Both the vertical and horizontal movement of this lead in soils has been assumed to be negligible due to the very high affinity of lead for various soil components. This has in general been the case, except where man has disturbed the soil through tillage, possibly leaving the Pb-soil complex exposed to potential wind or water-effected erosion. This movement is of course predominately horizontal.

In contrast to most plants, algae live predominantly in an aquatic environment where horizontal and vertical transfer of lead occurs with relative ease at low concentrations. Algae clearly show a capacity to concentrate lead by adsorption and absorption from their aquatic environment. The implications of this biomagnification for higher forms of life are not known. So far as effects of lead on algae are concerned, the inhibitory effects on growth and metabolic processes which have been noted all occur at lead levels in excess of 1 ppm. Such levels of water contamination seldom occur in nature, even with the added burden of pollution from lead mine tailings or municipal and industrial wastes.

Ascending to the world of lichen and fungi, one finds that the capacity for biomagnification disappears. This is because these plants reside in soils, which have a strong affinity of their own for lead. So far as toxic effects are concerned, the evidence is too sparse to arrive at any firm conclusions, but there is no evidence to encourage the belief that these forms of life are in any way threatened by the concentrations of lead they might encounter even when residing in close proximity to point or line sources of lead pollution.

The uptake of lead by vascular plants has received considerably more attention than has been the case with lower forms of plant life. Aquatic forms concentrate lead to a considerable extent, as do algae, probably mainly by adsorption. Terrestrial vascular plants, however, show no concentrative capacity, except for roots. As with lower forms of terrestrial plant life this is no doubt due to the strong lead-binding capacity of soil.

There is no question as to the potential toxicity for livestock of plants contaminated with lead, but in all documented instances the contamination has resulted from aerial deposition of lead from the fallout of lead smelters. Transfer of lead to forage via the root system has never been demonstrated to be a problem under either natural or soil-amended conditions. Even the growth of plants in sewage sludge does not seem to result in any significant elevation of plant lead content.

There have been a number of studies indicating that food crop yields are reduced by lead, but only in soils containing concentrations far in excess of what is ever likely to be encountered under field conditions.

As the world food supply dwindles, certain circumstances may arise in which relatively moderate lead contamination of soil might reduce plant yields. The most likely circumstance may be phosphorus deficiency. Most evidence now available indicates that probably most lead absorbed by plant roots is rapidly precipitated as a Pb-phosphate complex without translocation. Reports indicate that lead in varied situations binds to many cellular components, especially phosphate-containing membranes, nucleotides, nucleic acids, and organelles; and that it also binds in vitro to insoluble ferric hydroxide, is codeposited with Ca^{2+} in Pb-protein complexes and forms mercaptides with the -SH group of several amino acids. The significance of the predominant Pb-phosphate complexation is seen in studies with corn and several tree species where phosphate deficient plants exhibited a greater toxic response to lead. These observations could have future agricultural applicability since increases in land usage for agriculture will likely come with cropping of marginal lands, many of which are low in phosphorus. While suggestions have been made that a "healthy plant" can withstand most stress factors better than one which is already stressed, it seems that of all stresses which could have an impact on lead uptake and translocation in the plant, phosphorus deficiency may possibly be the most important.

There is still a need to determine how much lead in plant food is due to contamination on in the field and how much is due to various stages of processing and storage. No systematic study has ever been reported in which the flow of lead into and out of the raw plant food products has been delineated.

1.5 EFFECTS ON ANIMALS

There have been numerous studies reported concerning the occurrence and effects of lead in a broad range of animal species, both aquatic and terrestrial.

Many survey studies have been made on the concentrations of lead occurring in fresh and marine waters and in the aquatic species residing therein. As expected, experimental studies have shown that aquatic species accumulate lead when the concentrations of lead in their environment increase. There is no convincing evidence for biomagnification of lead in the aquatic food chain however.

Concentrations of lead shown to be toxic are considerably higher than that found to generally occur in natural waters. There is no evidence incriminating lead as producing adverse biologic effects in aquatic life in natural waters in the United States. Fish kills have been reported, however, as occuring in rivers near old lead mining areas in England. It was reasoned that the concentration of lead in the rivers would rise sharply whenever heavy rains effected leaching of lead from the surrounding areas.

It has been reported that methylation of lead can occur in an aquatic environment. A confirmation of this finding and a definition of the factors favoring the formation of this form of lead in an aquatic environment would be of considerable interest.

In insects, the concentration of lead reflects the concentration in the environment, as in aquatic animals. There is some evidence for biomagnification whereby lead is concentrated in its progression from plant foods to herbivores and on up to insect carnivores. Data concerning biological effects in insects are relatively sparse. Changes in gene frequency in *Drosophila* have been found to be significantly correlated with distance from a lead smelter in Missouri. Similar studies in other insect species have not been reported.

The impact of environmental lead on wildlife is difficult to assess with one notable exception. It is clear that waterfowl have died in large numbers resulting from the ingestion of spent lead shot. The problem has been recognized for years and extensive efforts have been made to find a substitute for lead shot. Soft iron approaches lead in suitability and for the past two years this shot has been required for hunting in certain flyways. Lead shot probably will be banned from even more flyways in future hunting seasons. Certainly this should have a favorable effect in reducing the incidence of lead poisoning in waterfowl. Hopefully, other problems will not be created instead. For example, will more birds be wounded instead of killed because of the less favorable ballistic qualities of soft iron? A few years ago, hardening of the soft iron was considered to be a real problem - with a resultant hazard to hunters in the forms of split gun barrels, especially if the shotgun were equipped with a full choke.

A number of survey studies have been made which show that increased body burdens of lead occur in terrestrial wildlife inhabiting areas contaminated with lead, e.g., roadsides, old apple orchards, and in the vicinity of industrial lead operations. There is no evidence that these increased body burdens of lead are causing deaths. The difficulties in determining population shifts, decreased life span, depressed growth or reproductive difficulties in most wild animal species are obvious. Even if such effects could be determined as occurring within localized areas of contamination, the significance relative to the population at large would be questionable.

An extensive body of information exists on clinical lead poisoning in domestic animals. The sources of poisoning, clinical signs in several species and gross and microscopic lesions have been described in many publications. Lead poisoning has been and still is a commonly diagnosed toxicologic problem in veterinary medicine. For example, 80 to 100 episodes are reported annually from the Texas Veterinary Diagnostic Laboratory. Lead poisoning accounted for 1.2% of all canine hospital admissions at the Angell Memorial Animal Hospital between 1969 through 1971. Thus, the ingestion of lead by animals in amounts sufficient to produce overt clinical poisoning is important.

The sources of lead in domesticated animals vary greatly depending on the environment and species peculiarities. Cattle are indiscriminate eaters and most any lead-containing material may be ingested (for example, paint, storage batteries, used motor oil and filters and certain types of grease and putty). Forage contaminated from industrial lead operations or mines has been incriminated as a source to cattle and also to horses and sheep. Dogs, like cattle, are indiscriminate eaters and will consume a variety of lead-containing materials (for example, plaster, paint, linoleum, and a variety of lead objects). The sources of lead described above have been documented repeatedly as being responsible for clinical cases of poisoning in animals.

There are other potential sources of lead to animals that have not until recently received serious consideration. These include the ingestion of soil by grazing animals and the addition of feed-grade mineral supplements to feed products. It is conceivable that the ingestion of lead-containing soil, in addition to the forage in certain areas, could result in the consumption of lethal quantities of lead.

Horses are suspected of consuming considerably more soil while grazing than cattle but studies designed to quantitate the amount ingested have not been made. Ingestion of soil might account for the enormous differences reported in toxic doses of lead to horses as compared to cattle, based upon forage content of lead. Studies designed to quantitate the amount of soil ingested by grazing horses should be most helpful in resolving this question.

Little definitive information is available on the effect of lead in domestic animals at levels that are elevated, but insufficient to produce poisoning. Limited data concerning cattle indicate that even when fodder contained 100 ppm Pb, there was no effect on feed consumption, weight gain, electrocardiogram patterns or respiratory rate. Examination of the cerebral cortex, liver and kidney cortex by electron microscopy did not reveal any ultrastructural changes. In another study (daily Pb doses of 5 to 6 mg/kg, corresponding to a concentration in excess of 200 ppm in forage) steers have been shown to grow normally for as long as 33 months. On the other hand, 15 mg/kg/day fed to steers for 283 days resulted in the development of anemia following the 42nd day of feeding, but no observable signs of lead intoxication were reported other than a slower rate of growth.

1.6 EFFECTS ON HUMANS

Evaluation of the hazards of lead exposure in man has been ongoing for many years. Largely as a consequence of this research, the incidence of illness and death attributable to lead has been drastically reduced, particularly during the past twenty years. Yet, for all that, research continues at an ever-accelerating pace. Some new subtle effects of lead are being reported. Just as lead in the environment has proven to be ubiquitous, so have the biological effects in mammalian systems. Needless to say, most current information has been obtained utilizing animal models and in many cases the doses of lead used to elicit responses have been extremely high. In some instances the human health implications of animal studies have been defined with a reasonable degree of certainty. In many other cases,well-designed studies in human populations have not been done.

Evaluation of toxicity requires specification not only of an effect, but also of the dose at which it occurs. In the broad sense of the word, dose includes all knowledge concerning transfer from the external environment to the receptor site where the toxic effect is elicited. Needless to say, the receptor site is usually either unknown or is not accessible for study in man. In the case of lead, the usual indirect measure of dose is the concentration of lead in the blood (PbB), conventionally expressed as μg Pb/dl. There is some knowledge as to how PbB relates to external doses *via* inhalation and ingestion. Much also is known about the relationship of PbB to degree of effect (dose-effect relationship) or to the incidence of occurrence of an effect (dose-response relationship). Thus, PbB forms a vital link between external dose and effect.

The major routes of absorption are the gastrointestinal tract and the respiratory system. Efforts to determine the absorption of lead by the human body at specified air lead concentrations have been only marginally successful for various technical reasons. It has been necessary to resort to PbB as an indirect measure of "dose" of air lead. For people who are breathing fairly constant air lead concentrations, averaged over months, the concentration of lead in the blood varies in accordance with the air lead concentration. Analysis of data as to air lead *vs*. PbB from several studies of adults indicate that over the range of general ambient air lead concentrations, 1 μg Pb/m^3 of air contributes 1-2 μg Pb per deciliter of blood. This relationship seems also to apply to children. At higher air lead concentrations, such as are encountered in industry, the incremental rise in PbB is lower per unit air lead concentration.

Direct determination of absorption of lead from the digestive tract is not beset with as many technical difficulties as is the case with inhaled lead. Although the number of studies of lead absorption performed in people is extremely limited, the conclusions drawn are fairly consistent. Approximately 8 percent of total, normal dietary lead is absorbed in adults and 40-50 percent is absorbed in the case of infants and preschool-age children. Dietary intake of lead in the general adult population is about 150-250 μg/d. Limited information suggests that every 100 μg Pb ingested in the diet daily contributes about 6 μg to PbB. Thus, diet is the principal source of lead under normal circumstances.

The relative contribution of various types of foods and beverages to PbB is poorly understood. It is not enough to know the concentrations of Pb in foods and the amounts consumed since bioavailability and absorption may vary considerably. Thus, for example, the lead in foods high in calcium is less well-absorbed than is the case when dietary calcium is low, and lead in beverages consumed on an empty stomach is absorbed to a substantially greater degree than lead in foods. Metallic lead particles such as are found in the side seam region of lead soldered cans is very poorly absorbed compared to lead acetate incorporated into the diet of experimental animals. The availability for absorption of lead in paint chips is of special concern because young children are known to chew and swallow paint chips. Animal studies suggest that lead in this form is substantially absorbed, though probably not as well as lead in foods.

The absorption of inorganic lead salts from the skin is negligible, even at high concentrations. Lead soaps used in industrial lubricants, however, are absorbed to a significant extent, probably because these soaps are lipid-soluble.

The fetus absorbs lead freely from its maternal environment. This is evident from numerous animal studies and some human autopsy studies. The maternal-fetal system tends to equilibrate as indicated by the fact that PbB's in the newborn correspond closely to the PbB's of their mothers.

Once absorbed, lead displays certain important features regarding distribution. Within the blood, lead is concentrated mainly in the erythrocytes. Among the soft tissue structures, the liver, kidney, and aorta have relatively high concentrations, whereas the concentration in brain, muscle and heart is relatively low. All of these differences are relatively minor, however, in contrast to the well-known propensity which lead has to accumulate in bone. Approximately 90 percent of the lead in the body of adults resides in the skeleton. The figure is lower for infants and young children.

Because of its slow rate of excretion, lead tends to accumulate in the body to middle life and beyond. Accumulation is more pronounced in some tissues and body fluids than in others. Thus, the concentration in the blood seems to reach a plateau early in life whereas in some tissues e.g., bone and large arteries, lead continues to increase to old age.

Excretion of lead is mainly by way of the urine and bile with losses from exfoliating dermal structures and sweat making only minor contributions to total excretion.

Mathematical models have been developed to describe the kinetics of lead distribution and excretion. So far as excretion is concerned, the most satisfactory model is a power function model. This says, in effect, that the rate of excretion of a single dose of lead becomes progressively slower with passing time. The model has not been rigorously tested.

The biological effects of lead in man are numerous. They occur at different levels of lead exposure, the body being more sensitive to some effects than to others. The critical organ is defined as the one exhibiting adverse effects at the lowest level of exposure and the critical dose (generally expressed as PbB) is the one causing the critical effect. Other biological effects, occurring at lower levels of lead exposure are termed subcritical effects. There is still some controversy as to which effect of lead is the critical one or, put another way, there is controversy as to the maximum level of lead exposure which produces no adverse effects.

It is perhaps useful to work downward from the worst effects which everyone will agree are adverse to those of uncertain health significance. In that regard, it is also useful to distinguish between clinical effects and subclinical effects. For the purposes of this review, clinical effects are those which a subject can perceive and which a physician would normally seek to correct. Subclinical effects are those which under normal circumstances do not result in a perceptible decrement in body function but which could possibly reduce an individual's capacity to cope with a coexistent body stress.

The principal organs and systems affected by lead are the kidneys, the hematopoietic system and the central and peripheral nervous systems. In all four cases a spectrum is seen, incuding both subclinical and clinical effects. In addition, at least one effect occurs in the hematopoietic system which is considered to be of dubious health significance and which therefore may be classified as "subcritical".

Prolonged elevated lead exposure results in two general types of kidney disease. The first affects the renal tubules and the second, commonly referred to as chronic lead nephropathy, is characterized by slow development of contracted kidneys with arteriosclerotic changes, interstitial fibrosis and glomerular atrophy. In contrast to renal tubular disease caused by lead, chronic lead nephropathy is relatively irreversible and has been shown to lead to renal failure and death in workers with heavy lead exposure.

The disease occurs too among heavy drinkers of lead-contaminated illicitly-distilled whiskey. There also is some evidence that heavy, prolonged lead exposure in childhood can cause death in middle life from chronic lead nephropathy. This particular form of the disease has been identified only in Queensland, Australia, from childhood exposure during a period of time limited to the turn of the century.

It seems from available clinical and epidemiological evidence that this disease occurs only when PbB's exceed 80 micrograms/dl for prolonged periods, although one report suggests that exposures of only a few years with PbB's below 80 may be sufficient to cause chronic lead nephropathy, at least in adults.

The renal tubular disease caused by lead is seen in heavily exposed adults and children. The intensity of lead exposure necessary to cause renal tubular disease is probably at least as high as is required to cause chronic lead nephropathy, although the duration of exposure required is perhaps shorter. Limited data indicate that the condition is readily reversed by treatment with chelating agents e.g., ethylenediamine tetraacetate (EDTA). The health consequences also probably are less severe than for chronic lead nephropathy. The disease state should nevertheless be classified as "clinical". It consists of elevated renal excretion of amino acids, phosphate, and glucose, conditions which a physician would probably seek to correct although they are not effects which normally would lead a subject to seek medical attention in the first place, at least not in the absence of other co-existent lead effects.

The effects of lead on the hematopoietic system are varied in nature. They include shortened survival of circulating red cells and decreased rate of hemoglobin synthesis in the bone marrow. Both of these general effects contribute to the anemia which is characteristic of lead poisoning. Anemia is clearly a clinical effect, one which a physician would normally seek to correct. The minimal level of lead exposure which is necessary to cause anemia is difficult to specify, if only because the clinical definition of anemia is imprecise. It is perhaps more to the point to consider the minimal level of lead exposure at which a downward drift in blood hemoglobin first appears, even within the accepted normal range. This minimal level appears to be PbB = 40 in children and PbB = 50 in adults.

Numerous specific biochemical defects are known to occur which may contribute to reduced circulating hemoglobin. Some are more lead-sensitive than others. Thus, inhibition of erythrocytic ATP'ase, which may contribute to a reduced lifespan of erythrocytes and inhibition of globin synthesis are effects which probably occur only at levels of lead exposure somewhat higher than for some other effects which concern the synthesis of heme.

Two enzymes in the pathway leading to heme synthesis are clearly inhibited by lead at PbB's below 40. The first of these is heme synthetase, a mitochondrial enzyme which catalyzes the final step in heme synthesis, the insertion of iron into protoporphyrin IX. Inhibition of this enzyme is reflected in the appearance of elevated protoporphyrin IX in circulating red cells, an effect which occurs at PbB's as low as 25 in adult males and as low as 20 in adult females and children. At even lower levels of lead exposure (PbB = 15), the enzyme aninolevulinic acid dehydratase (ALAD) which converts the heme precursor aminolevulinic acid (ALA) to the intermediate porphobilinogen (PBG) is somewhat inhibited, both in blood and in some other tissues. The consequence of inhibition of this enzyme is thought to be elevation of the precursor ALA in blood plasma and urine. This effect does occur, but only as PbB rises above 40. Thus, the significance of ALAD inhibition at very low levels of lead exposure is uncertain and is considered by most to be a subcritical effect.

The basic issue, for which there is no clear answer, is as to whether elevation of erythrocytic protoporphyrin between PbB = 20 and PbB = 40 is to be considered a critical or subcritical effect. The effect certainly is compensated since hemoglobin levels are sustained at a normal level in this range of lead exposure. The real issue is as to whether or not a person's capacity to cope with a co-existent stress on hematopoiesis is in any way compromised. Not much is known about this problem. There is a need for more research to determine the health consequences of this compensated state, and also to determine the implications of the effects of lead on the synthesis of other hemoproteins essential to normal body function. It has been shown that mixed function oxidase induction is reduced in lead exposure, suggesting an inhibition of synthesis of the hemoprotein cytochrome P-450. This effect, however, does not seem to occur at levels of lead exposure below those affecting the concentration of hemoglobin in the blood. Effects on other hemoproteins are virtually unknown.

There has been much controversy in recent years regarding the effects of lead on the central nervous system. The concern has its origins in the well-documented fact that very high lead exposure causes severe, often fatal damage to the brain in both adults and children. It is also known that attacks of lead encephalopathy in children and even severe lead poisoning in the absence of encephalopathy can give rise to long-term effects on brain function including mental retardation, altered sensory perception and slowed learning. Such cases have resulted from high exposures (PbB $\geq$ 80).

In recent years, there have been studies reported of possible neurological and behavioral effects of lead in children whose PbB's were in the range of 40-80. All of these studies have been retrospective in nature. The majority of them focused on comparison of children with high and low PbB's. In some cases, one or more PbB determinations were available at a point in time prior to the neurobehavioral test. Although most of these studies are flawed in one way or another, a number of them provide reasonably good evidence that PbB's in excess of 50 may result in impairment measured by sensitive psychometric tests. There also is fragmentary evidence to suggest that even moderately elevated lead exposure *in utero* may increase the occurrence of mental retardation. As with the studies performed on children with postnatal lead exposure, it is not possible to specify either the critical period or level of exposure required to induce deleterious effects. Finally, it should be pointed out that neurobehavioral effects may well be a result of the combined effects of lead and other stressors, both physical and social. All studies reporting lead effects have been conducted in socio-economically deprived populations.

The most satisfactory approach to problems of this type is the prospective study, wherein a continuing profile of dose and effect are available. Unfortunately, no such studies have been reported or, seemingly, are even underway.

Numerous laboratory animal studies of neurobehavioral effects of prenatal and perinatal lead exposure have been reported. Although numerous methodological problems have confounded the interpretation of these studies, it does appear that moderate lead exposure does result in locomotor and operant behavioral effects. Future studies are needed in which confounding variables, e.g., nutritional status and litter size are more closely controlled. Furthermore, multiple measurements of internal dose are needed in addition to PbB, e.g., protoporphyrin and ALA excretion in order to provide better interlaboratory comparison of data.

It should also be mentioned in passing that one laboratory has reported subtle neurobehavioral effects in lead-exposed industrial workers (PbB > 80). This study was beset with many methodological problems and equipment failures. A similar type of study conducted by another group of investigators was negative. Thus, for the present at least, the occurrence of subtle neurobehavioral effects of moderate lead exposure in adults is uncertain.

The peripheral nervous system also is adversely affected by lead. There are numerous reports of peripheral neuropathy in patients with clinical lead poisoning but not necessarily in conjunction with clinical neurological symptoms. Major effects reported are reduced nerve conduction velocity and electromyographic deficits. These effects have been reported to occur in both adults and children. Reduction of nerve conduction velocity without clinical evidence of neuropathy has also been reported. It is not certain at this time just where the lead exposure threshold for this effect lies, but it is probably at a PbB of about 50 in both adults and children. The effect must be considered adverse, particularly since certain factors may be additive to the lead-induced effect. Thus, alcoholism and diabetes also cause slowed nerve conduction, and there is some evidence of suggesting that presence of the sickle cell trait may constitute a special risk for this effect.

There are numerous other organs and systems in the body which are adversely affected by lead, but the information at hand is insufficient to make possible any judgements as to dose-effect and dose-response relationships.

Until more is learned about these effects, estimates of acceptable maximal lead exposure must rely on knowledge regarding effects on the hematopoietic system, the kidney and the nervous system. It seems clear that the kidney can be ruled out as the critical organ. Best estimates of threshold exposure even for subclinical effects on the peripheral nervous system indicate a PbB of about 50. On the other hand, the threshold for clinical effects on the central nervous system may be about 50. This threshold is therefore clearly the one of greater concern. It must be reiterated that estimated thresholds have validity only for the populations which have actually been studied. Since thresholds tend to fall progressively as sample size increases. The true threshold for effects on the central nervous system of all children critically exposed must be lower than applies to the sample. At present, it is impossible to state how much lower the population threshold is.

The dose-response relationships for lead effects on the hematopoietic system are much more clearly delineated than for any other lead effects,but again, any estimated thresholds are based on limited population samples. The only way to protect everyone from effects of poisons is to monitor everyone - an obvious impossibility.

The hematopoietic system is, so far as can be discerned, the most lead-sensitive system among the four under discussion, but which effect should be considered the critical one? If the rise in erythrocytic protoporphyrin is to be considered the critical one, as has been proposed by some, total lead exposure should be reduced to a point such that no woman or child's PbB rises above 20 and no man's PbB rises above 25. Judgment concerning the importance of achieving such a goal should be tempered by two considerations. In the first place, the effect is a subclinical one. Moreover, unlike the case with renal and, perhaps, neurobehavior effects, this one is reversible with reduction of exposure.

Some of the miscellaneous effects of lead for which no estimates of threshold are possible at present have been recognized for many years by numerous investigators. Others have been reported only by one or two investigators and therefore must be evaluated with appropriate reservations. Beyond that, there also are some effects which have been reported to occur in experimental animals and for which no human data are available.

It has long been known that lead causes colic. This effect occurs in men who show other clinical signs of poisoning concurrently, e.g., anemia. It seems unlikely therefore that this effect is particularly lead-sensitive. The cardiovascular system undoubtedly also is affected by grossly elevated lead exposure. The incidence of cerebrovascular deaths was reported to be elevated among lead workers exposed during the first quarter of this century but not among men exposed more recently. Hypertension has also been reported to occur as a result of heavy lead exposure, although a more recent study indicates that it does not occur under more recent industrial lead exposure conditions. Toxic actions on the heart have also been reported, but, again, only in cases of clinical poisoning.

During the latter part of the 19th century and on into the first quarter of this century there were numerous reports of a high incidence of miscarriages and stillbirths among women working in the lead trades. PbB's were not available at that time, but it is likely that women today only rarely, if ever, experience the high exposures which probably existed at that time.

There are single reports of ovulatory dysfunctions in women and of sperm abnormalities in men working in the lead trades. These effects were observed at relatively modest levels of elevated lead exposure. Further studies are needed.

There are scattered reports of other effects in man, such as chromosal absormalities in lymphocytes and impaired thyroid function. The health significance of these findings is obscure at present. Lead also has been reported to be teratogenic, but only on the basis of laboratory animal data.

Finally, the question of carcinogenicity has received some attention. Lead definitely is carcinogenic in the rat and mouse. In these species it causes renal adenomas and adenocarcinomas, but only at extremely high dose relative to any likely level of human exposure. The renal tumors have been reported by a number of independent investigators. There also is a single report of lead-induced gliomas in rats. Among three epidemiological reports of causes of death in people with elevated lead exposure, only one suggests a possible association with cancer. The authors of this last-named report conclude that even this association, of marginal statistical significance, is to be discounted so far as a causal relationship is concerned.

1.7 ENVIRONMENTAL DISTRIBUTION AND TRANSFORMATION

Lead is widespread as a natural constituent of rocks and soils. Even in areas most remote from human influences, the earth's crust contains approximately 16 ppm Pb. Human activity has caused some increase in the concentration of lead in the environment, particularly in and near large centers of human population. So far as soil is concerned, the areas of contamination are mainly the result of aerial transport from point sources such as smelters and from heavily-traveled highways. The zone of soil contamination extends only a few miles from smelters and only outward a few hundred meters from heavily-traveled roadways. Haulage of lead ores in trucks from mines to primary smelters is a minor additional source of roadside contamination occurring in a few very limited areas.

In spite of the highly restricted zone of detectable soil contamination, it would be incorrect to conclude that some long-range soil contamination does not occur. Analysis of lead in glacial ice, museum specimens of wildlife and plants, and successive rings of long-lived trees indicates that a substantial general dispersion of man-generated lead has occurred since the

Industrial Revolution. This is no doubt attributable to aerial transport from areas of technological activity. Transport models have as yet not been very well developed to describe this process of dispersion.

The specific sources of man-generated lead pollution are numerous. The major uses of lead are in the manufacture of storage batteries, antiknock additives for automotive fuels, pigments, ammunition and solder. Nearly one half of this lead originates from recycled metallic lead. U.S. production has remained fairly stable in recent years. There is a suggestion of a downward trend however, particularly in the categories of paint pigments and antiknock fuel additives. These downward trends are likely to continue because of restrictions on ambient air pollution and the use of lead in household paints.

Although only sixteen percent of lead production goes into the manufacture of fuel additives, it is estimated that combustion of lead-containing fuels accounts for almost ninety percent of aerial emissions and secondary contamination of soil, plants, and water by fallout. Among the several miscellaneous sources of aerial emission, primary and secondary lead smelters are of special concern. The fallout zone from these stationary sources is quite small in comparison to the total zone of contamination along all U.S. roadways. The gradient from source to baseline, however, is quite steep, with exceedingly high aerial and soil lead concentrations sometimes occurring in the immediate vicinity of the stacks. Although the degree of soil contamination in the smoke zone of some lead smelters may be greater than along highways, the total impact of highway fallout as a threat to the public health probably is the more important of the two. Nevertheless, concentrations of lead as high as in the immediate vicinity of smelters sometimes are reported for soils along major freeways.

Runoff from contaminated soils into water is extremely limited owing to the precipitation of lead salts and the binding of lead ions to stream sediment. There is a vertical gradient, however, of lead in oceans. Concentrations near the surface are much greater than in deep waters. Regional differences in surface concentrations are considerable. It is not clear as to how much of the gradient is attributable to fallout over the oceans as compared to runoff from streams. The median concentrations of lead in U.S. streams generally is reported to be less than 10 μg/ℓ.

Wastewaters entering treatment plants often have extremely high concentrations of lead (∿ 100-900 μg/ℓ) in contrast to streams and oceans. This probably mainly because wastewaters carry lead-bearing street dust heavily contaminated with near-fallout of gasoline motor exhuast. This dust often contains as much as 0.3 percent lead.

Although the lead content of city water supplies measured at the reservoirs seldom exceeds 50 μg/ℓ., water drawn from household taps often exceeds this level. This is mainly due to the use of lead water pipes and, worse, lead-lined water storage tanks. Low concentrations of dissolved solids (soft water) and an acidic pH exacerbate the problem. Under extremely unfavorable conditions the lead concentration may exceed 1000 μg/l., as in Glasgow, Scotland.

Perhaps the greatest single source of lead hazard to children is the presence of lead-base paint on the exterior and interior of private dwellings. Such surfaces are particularly hazardous when they are cracked or peeling. Most cases of clinical lead poisoning in infants and young children have been attributed to swallowing paint chips. The soil immediately surrounding houses coated with lead-base paints also may be heavily contaminated as a result of weathering. Although lead-base household paints have not been used extensively since the 1940's, the hazard persists in old, run-down neighborhoods. In such neighborhoods the number of pre-school children with unduly elevated lead exposure is alarmingly high. As it happens, traffic density and consequent soil and dust contamination also is generally high. A major unresolved issue today is as to the relative contributions to lead exposure of lead-bearing paint on the one hand and of lead-bearing dust and soil on the other. The child who engages in the licking, chewing and swallowing of foreign objects probably does not exhibit any preference for paint vs. soil and dust, although even that cannot be affirmed with any strong conviction. In any event, there is a great need today for research concerning the sources of lead in young children. It is not simply a question of establishing the relative importance of the suspect sources. It is also a question of determining the concentrations of lead in the several media which are minimally hazardous. Ultimately, decisions must be made as to which level of lead in each of the several media calls for remedial action.

1.8 ENVIRONMENTAL INTERACTIONS AND THEIR CONSEQUENCES

This final chapter brings together some elements of most previous chapters. It describes the movement of lead through the ecosystem with due attention to possible biomagnification phenomena. As a broad generalization, it seems fair to state that multi-stage biomagnification is not apparent in the case of lead in the environment. Several properties of lead account for this. To begin with, lead in most natural forms is relatively insoluble and does not therefore tend to move readily across biological membranes. For that matter, its insolubility tends to minimize its presence in water, the natural solvent which conveys nutrients into living systems. A further characteristic of lead tending to limit its transfer up the phylogenetic scale is its affinity for calcareous structures such as bones and shells. These elements in animal systems generally are rejected by predators, thereby diluting rather than concentrating lead in the food chain. This is not to deny that lead remains to this day a significant hazard to some forms of life. Rather, it is to say that current problems are one-stage or, at best, two-stage problems in which some inanimate form of lead interacts either directly with the target species or by way of one transfer medium. Thus, in the case of man and domesticated animals, lead is either inhaled or swallowed directly from contaminated air or water or it is swallowed with externally-contaminated food. Multiple stage transfer is not in evidence.

Transfer of lead from plants to herbivore to carnivore in the insect world seems to be an exception. Here there is evidence for biomagnification.

The major source of lead for the average person is probably food and beverages. This conclusion is based on two considerations. The first is in regard to the relative insignificance of the other major transfer medium-air. Few people inhale an average air lead concencration in excess of 2 μg Pb/m^3. At best, this contribution to circulating blood lead concentration is 4 μg Pb/dl. Assuming a normal PbB of 15 μg/dl, this leaves 11 μg Pb/dl to be accounted for. In the absence of any other widespread sources of lead intake for the average mean, foods and beverages are generally held responsible for the predominant remaining fraction of intake. It is therefore important to consider the extent to which lead in foods and beverages is reducible. Put another way, "To what extent are foods and beverages contaminated by lead introduced either in production or in processing?". The answers to this question are at present totally unsatisfactory. There are absolutely no studies available in which the raw product has been examined as to its inital natural lead content, its initial man-generated lead content and its addition and/or subtraction of lead in the course of processing and presentation to the consumer. Certain isolated segments of the overall problem have received attention. Thus, it is widely recognized that the soldered seams of cans are potential sources of food contamination. Certain foods have been found to double their lead content as a result of the transfer of lead from solder to filler, especially during storage for substantial periods of time. The significance of this transfer is still unknown, however. More information is needed as to (1) the total dietary contribution of such items and (2) the availability for absorption of the solder contribution. It is recognized that contamination from solder is in the form of microscopic pellets of metallic lead which are not nearly as readily absorbed from the gastrointestinal tract as is lead present in foods in the form of simple lead salts bound to natural ligands. There is a need to establish more clearly the bioavailability of solder-derived lead.

It has been found recently that canned pet foods have very high concentrations of lead. These products are sometimes purchased by the poor for human consumption. The source of this lead has not been determined.

2.0 PHYSICAL AND CHEMICAL PROPERTIES AND ANALYSIS

2.1 SUMMARY

Lead is a soft, malleable, ductile, dense, bluish-gray metal with a melting point of 372 C, and a boiling point of 1740 C. In the presence of moisture, lead is readily coated with an oxide film, which with carbon dioxide forms a basic white carbonate. Nitric acid converts lead to soluble lead nitrate. Lead is moderately resistant to both sulfuric and hydrochloric acids. In the presence of oxygen, most organic acids react with lead to form the corresponding organolead salts. Lead may be hardened by alloying with small amounts of metals such as antimony, arsenic and copper.

Most inorganic lead compounds are moderately to highly insoluble. This low solubility in the aqueous phase of natural systems affects the behavior of lead in the environment. As a consequence lead does not transfer readily from soil to plants or into bodies of water (see Sections 4.1;7.3.2, and 8.3.2). Similarly, lead tends to accumulate wherever it is delivered and consequently can become a hazard.

Of the organolead compounds, tetraethyllead and tetramethyllead (antiknock additives in gasolines) give rise to most of the lead that is released into the atmosphere as a result of their combustion in the automobile engine. The many other organic derivatives of lead are of minor importance compared to the lead tetraalykyls.

For the determination of lead concentrations in biological and environmental samples, each sample type presents a different analytical problem. As a result, much effort has been expended in developing suitable techniques for the measurement of lead. Great care must be exercised in all steps involved in lead analysis if reliable results are to be obtained. Sampling methods and materials should be selected which will not introduce elements that will interfere with the lead analysis. Lead-free storage containers should be used and appropriate preservatives should be added to the sample for storage purposes.

As the first step in the analysis, sample preparation should be adapted to the type of material being analyzed. The Association of Official Analytical Chemists has adopted the wet ash extraction procedure (digestion) as the preferred method. However, dry and bomb ashing methods have proven suitable for some samples. Nondestructive methods and methods of separation and preconcentrations based on density gradients and magnetic separation have been used where preservation of the identity of the lead compounds has been important.

For the actual lead determination, the colorimetric method based on dithizone was the standard method for lead analysis in all types of samples for many years. However, because of the need for rapid and reliable methods for blood lead analysis in screening people for lead exposure, the atomic absorption method (flameless technique) has generally become the method of choice.

Optical emission spectrometric analysis for lead can cover wide concentration ranges and is suitable for direct analysis of numerous types of samples, including soils, dried tissues, and solutions containing microgram quantities of lead. With a plasma source, this method can be used for rapidly measuring nanogram (10^{-9}) levels of lead. Electrochemical methods such as polarography can be used to determine lead accurately at the nanogram level. Other methods for lead determination are spark source mass spectometry, X-ray fluorescence, and activation analysis.

A considerable number on inter- and intralaboratory comparisons have been carried out on a variety of environmental samples to detect sources of error in the analytical procedures for lead. The results of these programs show that extreme care is required throughout the entire procedure to achieve high correlations among laboratories. The discrepancies among results from different laboratories have often been attributed to sample handling problems and to laboratory bias.

Interpretation of analytical results is complicated by the fact that at the trace level concentrations being analyzed, analytical methods are not yet available to determine the chemical form(s) in which lead is present. Satisfactory analytical techniques have not been developed for determining individually the organic and inorganic lead that may be present in tissue. Thus, except at macroconcentrations, results as reported are for total lead.

2.2 PHYSICAL AND CHEMICAL PROPERTIES

Lead is a soft metal with a bluish-gray color when freshly cut. Its bright luster soon disappears upon exposure to air because of the formation of lead oxide. The important physical constants of lead are presented in Table 2.1. It is atomic number 82 in the periodic classification of the elements, and has several naturally occurring isotopes which result in an average atomic weight of 207.19. Because lead has four electrons in its outer shell, it falls in Group IV of the periodic table, and consequently, might be expected to show a normal valence of +4 in its compounds. However, the 2 "s" electrons are difficult to ionize so the usual valence of lead in ionic compounds is +2 rather than +4. In acid solutions lead is a fair reducing agent; in alkaline solutions it is a rather strong reductant. The more important oxidation-reduction potentials for lead and its compounds are presented in Table 2.2 (Latimer, 1952).

Lead has good resistance to neutral solutions where the oxide and carbonate are the corrosion products, and is fairly resistant to alkaline solutions. Lead is resistant to sulfuric, sulfurous, phosphoric and chromic acids,

Table 2.1 PHYSICAL CONSTANTS FOR LEAD[a]

Melting point, C	347.43
Boiling point, C	1740
Specific gravity, at 20 C	11.3437
at 327.43 C	10.686
at 650.0 C	10.302
at 850.0 C	10.078
Vapor pressure, at 987 C, mm Hg	1.0
at 1167 C	10.0
at 1417 C	100.0
at 1508 C	200.0
at 1611 C	400.0
Surface tension, at 350 C, dyn/cm^2	442
at 400 C	438
at 500 C	431
Viscosity, at 441 C, cp	2.116
at 551 C	1.700
at 703 C	1.349
at 844 C	1.185
Specific heat, at 0 C, cal/g	0.0297
at 20 C	0.0306
at 100 C	0.0320
at 327 C	0.0390
at 500 C	0.037
Latent heat of fusion, cal/g	5.86
Latent heat of vaporization, cal/g	203
Thermal conductivity, at 20 C, cal/(cm^2) (C/cm) (sec)	0.083
at 100 C	27.021
at 327.43 C	94.6
at 600 C	107.2
at 800 C	116.4
Magnetic susceptibility, 10^{-6} egs units	0.12
Brinell hardness (cast)	4.2
Element bond length, Pb-Pb- at 25 C, Å	3.5003
Electrical resistivity, micro-ohms/cc at 20 C	20.648
Refractive index, sodium light	2.01
Velocity of sound, cm/sec x 10^5	1.227
Tensile strength, lb/sq in at 20 C	1920
Linear coefficient of expansion, per C x 10^{-5}	2.93

[a] Adapted from McKay. In: Encyclopedia of Chemical Technology, Vol. 12, A. Standen (ed.), Used by permission of Interscience Publishers, New York. (c) John Wiley and Sons, Inc., 1967.

Table 2.2 OXIDATION-REDUCTION POTENTIALS FOR LEAD[a]

Reaction	$\Delta E°$, volts
$Pb \rightarrow Pb^{+2} + 2e$	+ 0.126
$Pb^{+2} \rightarrow Pb^{+4} + 2e$	- 1.7
$Pb + SO_4^{-2} \rightarrow PbSO_4 + 2e$	+ 0.356
$Pb + 2OH^- \rightarrow PbO + H_2O + 2e$	+ 0.58
$Pb^{+2} + 2H_2O \rightarrow PbO_2 + 4H^+ + 2e$	- 1.455
$PbSO_4 + 2H_2O \rightarrow PbO_2 + 4H^+ + SO_4^{-2} + 2e$	- 1.685
$PbO + 2OH^- \rightarrow PbO_2 + H_2O + 2e$	- 0.248
$Pb + 2Cl^- \rightarrow PbCl_2 + 2e$	+ 0.268
$Pb + 2Br^- \rightarrow PbBr_2 + 2e$	+ 0.280
$Pb + 2I^- \rightarrow PbI_2 + 2e$	+ 0.365
$Pb + S^{-2} \rightarrow PbS + 2e$	+ 0.980

[a] *Adapted from* Latimer, The Oxidation State of the Elements and Their Potentials in Aqueous Solutions, 2nd Edition, (c) 1952, pp 151-155. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, New Jersey.

but it is moderately attacked by hydrochloric and hydrofluoric acids. It is strongly corroded by nitric, acetic and formic acids and moderately affected by organic chlorides and aqueous solutions of metal chlorides. In the presence of oxygen most organic acids react with lead to form the corresponding organolead salts (Hamner, 1974).

The equilibrium model for the chemistry of aqueous lead developed by Stumm and Morgan (1970) indicates that at low pH and low pe (reducing conditions) elemental lead can be readily dissolved. This has health implications, where soft water with little or no buffering capacity is at a low pH and lead piping is used for potable water. Excessive lead concentrations in such water have been observed in Great Britain and in certain locations in the U. S. (see Section 7.3.2).

Lead's high density (11.3 grams per cubic centimeter), its softness, and relatively low melting point enable easy forming and casting. These physical characterists account for the numerous uses of lead (see Section 7.2). Lead forms low-melting alloys with tin, arsenic, antimony, bismuth, cadmium, and calcium, singularly and collectively. These alloys are fabricable by commercial processes (Hack, 1967). Alloys are also made from secondary lead which is recovered from scrap. Lead does not readily alloy with zinc, iron, nickel, and other high-melting metals. Alloys of lead can be extruded, drawn, rolled, cast, stamped, spun, and applied as a coating to other metals by hot dipping, electroplating, or spraying (Lead Industries Association, 1952). Thick layers of lead can be bonded to steel and other metals.

Refined primary lead is at least 99.85 percent pure; however, the impurities making up the balance put it into four different grades which in turn govern its use. "Corroding grade" lead (99.94 percent) is used in the manufacture of lead oxide for storage batteries and for pigments. The grades designated as "chemical" lead and "acid-copper" lead are more generally used for sheets and pipes in chemical installations because the small amount of copper and silver present increase the strength and corrosion resistance. The fourth grade "desilverized" lead, is used in general applications and in the manufacture of alloys.

2.2.1 Inorganic Compounds of Lead

The divalent lead compounds resemble those of the alkaline earth elements. The sulfate, nitrate, and carbonate compounds of lead are isomorphic with the corresponding barium and strontium compounds. Many lead compounds have two or more crystalline forms. The common inorganic compounds of lead (nitrate, chlorate, and acetate) are water-soluble; the chloride is sparingly soluble; and the sulfate, carbonate, chromate, phosphate, and sulfide are insoluble.

Values for the solubilities of common inorganic compounds of lead are presented in Table 2.3 (Lange, 1961; Weast, 1974). Lead sulfide has a very low solubility (approximately 0.8 mg/l) and its formation can serve as a convenient method for the removal of lead from aqueous systems. Its solubility is higher than might be expected on consideration of the low solubility product ($Ksp = 7 \times 10^{-29}$). This is due mainly to the hydrolysis of the sulfide ion. (Kolthoff, et al., 1964).

Table 2.3 SOLUBILITIES OF INORGANIC COMPOUNDS OF LEAD[a,b]

Compound		Water Solubility, g/100 ml	Temperature, C
Name	Formula		
Acetate	$Pb(OOCCH_3)_2 \cdot 3H_2O$	44.3	20
Bromide	$PbBr_2$	0.844	20
Carbonate	$PbCO_3$	1.1×10^{-4}	20
Chlorate	$Pb(ClO_3)_2 \cdot H_2O$	151.3	18
Chloride	$PbCl_2$	0.99	20
Chromate	$PbCrO_4$	5.8×10^{-6}	20
Fluoride	PbF_2	0.064	20
Hydroxide	$Pb(OH)_2$	0.0155	20
Iodide	PbI_2	0.063	20
Nitrate	$Pb(NO_3)_2$	56.5	20
Oxalate	$Pb(OOC)_2$	1.6×10^{-4}	18
Oxide, mono-	PbO	1.7×10^{-3}	20
Oxide, tetra-	Pb_3O_4	5.3×10^{-5}	20
Phosphate	$Pb_3(PO_4)_2$	1.4×10^{-5}	20
Sulfate	$PbSO_4$	4.25×10^{-3}	25
Sulfide	PbS	8.6×10^{-5}	20

[a] Reprinted with permission from Handbook of Chemistry, 10th edition, N.S. Lange (ed.) (c) McGraw-Hill Book Company, 1967.

[b] Reprinted with permission from Handbook of Chemistry and Physics, 55th Edition, R.D. Weast (ed.). (c) CRC Press, Inc., 1974.

Santillan-Medrano and Jurinak (1975) found that the solubility of lead in noncalcareous soils appeared to be regulated by $Pb(OH)_2$, $Pb_3(PO4)_2$, $Pb_4O(PO_4)_2$, $Pb_5(PO4)_3OH$, and was dependent on the pH. In calcareous soils $PbCO3$ was also significant. Reductions in lead uptake by plants of up to one-half in the presence of excess phosphate have been observed (see Sections 4.3.1.1 and 4.3.2.1).

Lead monoxide (PbO), one of the most important industrial lead compounds, exists in two forms. At ordinary temperatures, the monoxide exists as reddish-yellow, tetragonal crystals commonly referred to as litharge. At 480 C this transforms into yellow orthorhombic crystals known as massicot. Neither form of the oxide is appreciably soluble in water. Litharge dissolves only to the extent of 0.0017 gram/100 ml of water at 20 C, and massicot, 0.0023 gram/100 ml. The melting point of PbO is 888 C; it has appreciable volatility below this. PbO reacts readily with all common acids to form the corresponding salts and dissolves in alkali, though with more difficulty. Hence, PbO serves as a starting point for the preparation of many lead compounds (Thompson, 1967). The major uses of the inorganic and organic compounds of lead are discussed in Section 7.2 (see also Table 8.1).

Red lead, Pb_3O_4, contains both divalent and tetravalent lead atoms in a complex crystalline structure. It is prepared by the oxidation of PbO in air at 500 C.

Lead dioxide, PbO_2, is dark brown solid in which the lead atoms are tetravalent. It is a vigorous oxidizing agent when heated (290 C). PbO_2 can be produced in the laboratory by the anodic oxidation of solutions of lead compounds. Commercially, it is produced by the treatment of an alkaline slurry of red lead with chlorine (Klug and Brasted, 1958).

2.2.2 Organic Compounds of Lead

Organolead compounds are those in which the lead atom is bound directly to one or more carbon atoms. Since Lowig's first synthesis of an organolead compound in 1953, organolead chemistry has developed into one of the largest areas of organometallic chemistry. It has been estimated that about 1200 organolead compounds were known in 1965 (Shapiro and Frey, 1968). Only a few of these achieved commercial status.

The tetraorganolead compounds in which a tetravalent lead atom is bonded to four organic groups through a carbon atom represent the most stable class of organolead compounds. The four organic groups may be alkyl, aryl, cycloalkyl, arylalkyl, thienyl, furyl and substituted derivatives thereof. The most important of these compounds are the fuel additives, tetrathyllead (TEL) and tetramethyllead (TML).

In general, the alkyl derivatives of lead are highly toxic compounds, and are readily absorbed through the skin (see Section 6.2.1.2.3 and 6.3.2.3). TEL and TML are clear, colorless liquids, volatile, nonpolar, nonionic, and soluble in many organic solvents such as hydrocarbons, chloroform, ether, and absolute ethanol. They have very low water solubilities, and are relatively unreactive in air, water or alkali (Shapiro and Frey, 1968). They are, however, light-sensitive and undergo photochemical decomposition when they reach the atmosphere; because they are readily broken down by light and heat, their presence in the atmosphere is transient (National Academy of Sciences, 1972).

At 50 millimeters of mercury, TEL boils at 108.4 C, and TML at 33.2 C. TML decomposes on heating at 265 C, and TEL at 100 C (Shapiro and Frey, 1968). Some of the other physical properties, as summarized by Gerarde (1964), are presented in Table 2.4.

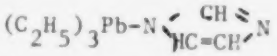
These compounds decompose readily during the combustion process, thus freeing the radicals to prevent the extremely rapid burning of gasoline. The so-called "regular" gasoline contains 3 to 4 milliliters of the tetralead compounds per gallon. This concentration represents from 2 to 3 grams of lead per gallon. To scavenge the lead from the engine, standard antiknock fluids also contain ethylene dibromide and/or ethylene dichloride. The chief lead emission products are (in particles of equivalent diameter between 2 and 10 micrometers) lead bromochloride ($PbCl \cdot Br$) and (in particles smaller than 1 micrometer) the alpha and beta forms of ammonium chloride and lead bromochloride ($NH_4Cl \cdot 2PbCl \cdot Br$, $2NH_4Cl \cdot PbCl \cdot Br$), minor quantities of lead sulfate ($PbSO_4$) and the mixed oxide and halide ($PbO \cdot PbCl \cdot Br \cdot H_2O$ National Academy of Science, 1972). These combustion products, present as solids, are the largest source of atmospheric lead pollution.

In addition to the tetralead derivatives, other types of organolead compounds are of environmental significance, for example, hexamethyldilead, which consists of six organic groups surrounding a pair of lead atoms:

$$(CH_3)_3Pb{-}Pb(CH_3)_3.$$

Lead can also be bonded to organic groups through an oxygen atom giving rise to a variety of alkoxides, such as trimethyllead methoxide, $(CH_3)_3PbOCH_3$. Peroxide structures are also known, for example, tert-butyl trimethyllead peroxide, $(CH_3)_3\ PbOOC(CH_3)_3$ (Shapiro and Frey, 1968).

A large number of organolead compounds also are known in which the lead is bonded to sulfur, for example, $(CH_3)_3PbSCH_3$. A few compounds have been prepared in which the sulfur is replaced by selenium or tellurium. Organolead compounds in which the lead is bonded to nitrogen are types in which the nitrogen is part of a heterocyclic ring:



$$(C_2H_5)_3Pb{-}N\begin{matrix} \diagup\ CH = \\ \diagdown HC{=}CH \diagup \end{matrix}N$$

(Shapiro and Frey, 1968).

Very recently evidence has been presented (Wong, et al., 1975) for the biotransformation of inorganic and organic lead into a tetraalkyl lead by microorganisms in lake sediments (see Section 3.2.1).

Table 2.4 PROPERTIES OF TETRAETHYLLEAD AND TETRAMETHYLLEAD[a]

Physical Properties	Tetraethyllead	Tetramethyllead
Physical form	Watery white oily liquid	Watery white oily liquid
Chemical formula	$(C_2H_5)_4Pb$	$(CH_3)_4Pb$
Odor	Faint, fruity	Faint, fruity (probably odorless in chem. pure state)
Saturated liquid density at 20 C	1.65 g/ml	1.99 g/ml
Vapor pressure at 20 C	0.27 mm Hg	22.5 mm Hg
Boiling point	199 C	110 C
Freezing point	130.2 C	30.3 C
Flash point (open cup)	85 C	About 38 C
Viscosity at 20 C	0.87 cps	0.53 cps
Refractive index nD^{20}	1.520	1.512
Solubility in water at 22 C	0.18 ppm	18.0 ppm
Solubility in gasoline	Soluble in all proportions	Soluble in all proportions

[a] Source: Gerarde. Reprinted with permission from Annual Reviews Pharmacology. (c) Annual Reviews, Inc., 1964.

2.2.3 Isotopes of Lead

There are four stable isotopes of lead, with the following abundances (Lederer, et al., 1967):

Isotope	Percent
Pb-204	1.4
Pb-206	25.1
Pb-207	21.3
Pb-208	52.7

Pb-204 has no radioactive progenitor. The Pb-206, Pb-207, and Pb-208 are produced by the radioactive decay of uranium-238, uranium-235, and thorium-232, with half-lives of 4.5,0.7, and 14 billion years, respectively (Lederer, et al., 1967). There are four radioactive isotopes of lead occurring as members of these decay series. Pb-211, Pb-212, and Pb-214 have short half-lives 36.1 min., 10.64 hr., and 26.8 min., respectively. Pb-210 (Radium-D), the longest lived, however, has a half-life of about 20 years, sufficiently long to be useful in environmental studies.

The stable isotope composition of naturally-occurring lead ores varies, depending on their geological evolution, and this can be used to determine the geological age of lead deposits. The isotopic composition may also be used to determine the sources of lead contamination (see Section 7.2). However, because lead is so durable and so much of it is recycled, the pool of recycled scrap and products derived from it (e.g., TEL) tends to average toward a fairly uniform composition. While this complicates the tracing of the orgin(s) of environmental lead by isotopic ratio measurements, the technique has still proven useful.

2.3 ANALYSIS FOR LEAD

The variety of environmental samples is so great as to pose a different analytical problem for each type of sample. Testing and surveillance of potentially exposed persons require methods indicative of lead poisoning which are reliable and rapid; biological samples pose their own distinctive problems.

Accurate determination of metals at the nanogram level exerts demands upon investigators in their attempts to prescribe emission limits of harmful materials and, more importantly, to understand the effect of these emissions upon people. The complexity of environmental and biological samples to be analyzed for trace levels of lead requires the utmost care in sampling, storage, preparation, and analysis in order to obtain meaningful results. In any analysis step lead can be lost or contamination occur to produce erroneous results. Probably the greatest error occurs during the decomposition of the sample for purposes of converting the lead to a form suitable for the analysis. The decomposition may require hours of digestion or ashing. This phase should be done in clean rooms, using clean reagents and vessels.

The following information represents steps being utilized in the search for better and simpler methods and techniques for assessing lead contents in a wide range of materials. Not only are systematic approaches being taken in the preparation of difficult samples where needed, but also direct sample analyses are being made as more sensitive methods of analysis are developed.

Awareness of reliability problems associated with all phases of the analytical processes including sampling, storage, and preservation, chemical treatment, and analysis has become evident.

2.3.1 Sample Storage and Preservation

Sampling techniques and conditions should be used which will collect samples representative of the problem under study. For ambient air sampling, Sawacki (1975) points out the difficulties experienced with filtering techniques used to collect particulate lead near highways. Variations in sampling techniques, involving different filter materials or the use of scrubbers, produced variation in the lead contents obtained due to variations in the efficiences of the collection media used. Similar variations can occur in sampling biological tissues unless steps are taken to homogenize the sample.

Attendant to sampling, the preservation of the integrity of the sample during the interim between collection and analysis is an absolute requirement. This is especially so for samples in forms which are susceptible to change, e.g., water or some biological samples. The primary consideration in these instances is to store the samples in previously cleaned and inert containers to prevent loss by absorption and diffusion or contamination by desorption from the container wall (U. S. Environmental Protection Agency, 1974). These considerations should apply as well to the digested concentrates in preparation for analysis.

The use of unclean containers for storage of either raw or chemically-treated samples can produce unpredictable results. It has been shown (Issaq and Zielinski, 1974) that considerable loss of lead, as aqueous $Pb(NO_3)_2$, occurred in less than 1 hour when stored without a stabilizing agent in materials such as Pyrex, Kimax, or polyethylene. Hydrogen peroxide was preferred for this. The stability of lead chelates was investigated (Kinrade and Van Loon, 1974), and it was found that the combined use of two agents, ammonium pyrrolidine dithiocarbamate (APDC) and diethylammonium diethyldithiocarbamate (DDDC) provide indefinitely long stability compared to the rapid deterioration when only one (APDC) was used. A similar multichelation treatment of water samples (Sachdev and West, 1970) produced stable lead solutions that were made slightly acidic.

Whole blood and urine samples (National Academy of Sciences, 1972) are best collected and used in polypropylene, Teflon, or other lead-free materials. A study of the effect of the aging of blood on the recoverability of lead (Mitchell, et al., 1972) was performed using blood stored at three different temperatures. Sample storage at 9 C was recommended on the basis of stability. Additional information indicates that after the addition of sufficient quantities of heparin, blood can be stored at room temperature for weeks (Braztel and Reed, 1974). In the frozen state, blood was not observed to deteriorate (Lerner, 1975)

Preservation of delta-aminolevulinic acid, an indirect indicator of the presence of lead in urine specimens, was accomplished by acidifying, refrigerating, and storing in the dark (Vincent and Ullman, 1970). A good review of the precautions to be taken in the sample treatment of biological fluids is available (Anand, et al., 1975).

2.3.2 Preparation of Samples for Analysis

The criteria for trace metal analytical methods are specificity, sensitivity, and precision. The achievement of these goals on samples containing the substances sought in the nanogram range often requires the use of separation and preconcentration techniques to avoid spurious results.

Although beset with the everpresent possibility of analyte loss or gain, most environmental samples are subjected to some form of chemical treatment. The purpose of chemical treatments is to provide an analyte concentration that is within the best range for good precision of the method and to reduce possible interferences from the matrix components. A thorough description of the destruction of organic matter in biological samples was given by Gorsuch (1970). Reference is also made to another review by Tölg (1972) which details a large number of chemical treatments for a variety of sample types.

Table 2.5 lists some typical concentration/separation procedures used for isolating the lead content of a number of different sample types. The amount of literature directed toward both treatment and analysis of many types of samples for lead is extensive. Investigators have determined beneficial measures for reducing decomposition times and background blanks. Some of these changes are presented below under the various sample types.

2.3.2.1 Biological Samples - -

The wet ash digestion procedure reported for plants and animal products (Hoover, et al., 1969) was adopted as the AOAC (Association of Official Analytical Chemists) preferred method (Horwitz, 1975) after testing its ruggedness in an interlaboratory comparison. Precautions are taken to insure the complete co-precipitation of lead with strontium sulfate. This procedure may be applicable to other biological samples requiring preconcentration procedures.

Both wet (digestion) and dry ashing procedures have been used for destroying the organic matrix of biological samples (Yeager, et al., 1971). These workers obtained similar results using either approach, but preferred dry ashing (as did Sutton, 1975) in silica dishes for reduced treating times.

However, as Tolg (1972) points out, dry-ashing in a muffle furnace at 400-800 C in the presence of air can lead to more or less loss of many elements, including Hg, B, Pb, Zn, Cd, Ga, In, Tl, As, Sb, Fe, Cr, and Cu. The addition of fluxes such as sulfur, phosphates, or sulfuric acid, reduces the losses in many cases, but magnifies the risk of raising the blank value. Interaction between the flux and the vessel - such as formation of insoluble silicates from silica and porcelain - and the formation of difficulty-soluble oxides, causes losses, which, together with the other disadvantages, render

Table 2.5 TYPICAL CONCENTRATION AND SEPARATION PROCEDURES USED IN DETERMINING LEAD IN A VARIETY OF ENVIRONMENTAL SAMPLES

Sample	Matrix Separation	Reagents or Conditions	Second Separation	Reagents or Conditions	Extraction	Reagent	Pb Specie Desired	Overall Treatment Time, hr	References
Plant and animal products	Wet ash	$HClO_4$, HNO_3, H_2SO_4	Salt conversion	$(NH_4)_2CO_3$	-	-	Total	4	Hoover et al.,(1969)
Biological									
Bone	Dry ash	500 C/Silica dishes	Chelation	APDC[b]	Solvent	MIBK[c]	Total	12	Yeager et al.,(1971)
Tissue	Dry ash	500 C/Silica dishes	Chelation	APDC[b]	Solvent	MIBK[c]	Total	12	Yeager et al.,(1971)
Blood	Dry ash	500 C/Silica dishes	Chelation	APDC[b]	Solvent	MIBK[c]	Total	12	Yeager et al.,(1971)
Urine	Dry ash	500 C/Silica dishes	Chelation	APDC[b]	Solvent	MIBK[c]	Total	12	Yeager et al.,(1971)
Feces	Dry ash	500 C/Silica dishes	-	-	-	-	Total	12	Yeager et al.,(1971)
Hair	Dry ash	500 C/Silica dishes	-	-	-	-	-	-	Clarke and Wilson (1974)
Water	Chelation	DDC[a]/APDC[b]	-	-	Solvent	MIBK[c]	Soluble	2	U.S. EPA (1974)
	Ion exchange	Resin-Dowex 1	Evaporation	Heat	-	-	Soluble	2	Korkisch and Sorio (1975), Mark et al. (1969)
Ambient air									
Filter (paper)	Dry ash	500 C	Evap.-diss.	$HF-HNO_3$	-	-	Inorganic	<4	Kometani (1972)
Filter (paper)	Wet ash	HNO_3, $HClO_4$	-	-	-	-	Inorganic	>4	Kometani (1972)
Filter (paper)	LTA[d]	Ionized O/100 C	Evap.-diss.	$HF-HNO_3$	-	-	Inorganic	<4	Kometani (1972)
Filter (glass)	Leach	HCl, HNO_3	Evap. to low vol.	Heat	-	-	Inorganic	12	Thompson et al., (1969)
Filter (cellulose)	Wet ash	HNO_3-HClO_4	Chelation	Dithizone	-	-	Inorganic	1	Annual Book of ASTM Standards (1972)
Soils	Leach	$HCl-HNO_3$ or $H_2SO_4-HNO_3$	-	-	-	-	Adsorbed	24	Anderson (1974)
	Fusion	$Na_2CO_3-KNO_3$	Ion excahnge	Chelex 100	-	-	Total	2	Freudiger and Kenner (1972)
	Bomb dissolution	$HF-HNO_3$	Electrochemical	Cathodic-anion	-	-	Total	3	Arden and Gale (1974)
Ceramics	Leach	Acetic acid	-	-	-	-	Acid-extractable	2	Krinitz (1974)
Organic lead									
Liquid fuels	Complexation	ICl	-	-	Solvent	MIBK[c]	Organic Pb	2	Campbell and Palmer (1972)
Ambient air	Adsorption	Charcoal	Leach/digestion	HCl, HNO_3, $HClO_4$	Chelation	Dithizone	Organic Pb	24	ASTM (1972)
Paints (solids)	Leach	HNO_3	-	-	-	-	Organic Pb	2	Eider (1971); Holak (1975)
Paints (liquids)	-	-	-	-	Solvent	MIBK[c]	Organic Pb	1	Eider (1971)

[a] Diethyldithiocarbamate.
[b] Ammonium pyrrolidine dithiocarbamate.
[c] Methylisobutylketone.
[d] Low temperature ashing.

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these procedures unsuitable for extreme trace analysis. Alternatively, Tolg describes a method of low temperature ashing between 100 and 200 C in a stream of oxygen with excitation by a high-frequency electromagnetic field.

Abu-Samra, et al., (1975) point out that wet-ashing methods seem to have gained greatest acceptance among workers interested in trace metals analysis. Abu-Samra and his co-workers developed a procedure for rapid, safe, and efficient ashing of biological samples using microwave heating. Complete digestion was accomplished in minutes. Human tissues were solubilized in a comparatively short time (2 hours) when treated with alcholic tetramethyl ammonium hydroxide (Gross and Parkinson, 1974).

Another technique intended to reduce the decomposition time of biological materials is the bomb method (Paus, 1972). Initial work indicated this to be comparable to wet ashing for the recovery of lead in seaweed and fish. This procedure also dissolves all the fats and proteins which are more difficult to decompose when using other concentration techniques. The presence of oils in the concentrates may interfere with the subsequent chelation of lead and with the flame characteristics when the sample is nebulized for atomic absorption spectroscopy (AAS).

A relatively rapid ion exchange technique recovers lead efficiently from dilute solutions of blood and urine, and also from their acid leachate solutions for analysis by atomic absorption (Lyons and Quinn, 1971).

Tracer studies were conducted to identify sources of error in the recovery of lead in blood samples via several preparation techniques (Kopito, et al., 1974). The lead isotope (^{203}Pb) was added as the nitrate or acetate. The four concentration techniques tested were two procedures of protein precipitation with trichloracetic acid (TCA) and subsequent chelation and extraction; acid digestions using TCA; and acid digestion coupled with coprecipitation with bismuth. The final concentrates of these procedures were analyzed using atomic absorption spectroscopy.

The experiments with the use of TCA singly showed that long incubation periods (1 hour) are required for quantitative recoveries. Incubation periods of short duration (10 minutes) yielded recoveries of only 85 percent, necessitating sucessive precipitation treatments. The procedure using TCA-mixed perchloric acid reagent resulted in only 75 percent recovery of the isotope. For the wet ashing procedure, using a mixture of nitric and perchloric acids at a termperature of 150 C, total recovery of the tracer was found. In uncovered beakers, lead contamination due to atmospheric fallout was observed. Also, complete destruction of the organic matter is necessary for efficient recovery of lead using the coprecipitation approach. This was made evident in studies involving tracer injection into mice followed by analysis of their blood.

2.3.2.2 Aqueous Samples--

In waters containing high amounts of humus lead may be present as a metallo-organic. The humus may reduce the efficiency of extraction of lead in some instances (Paus, 1971). This work compared direct water analyses with those obtained from the various extractive techniques (such as chelation and ion exchange) after destroying the humus content. The combined extractive and analytical techniques can provide specific lead specie estimation as to ionic, metallic or organic.

Ion exchange, resin-loaded papers have been used to separate the lead in waters for analysis by X-ray fluorescence (Lochmuller, et al., 1974). Low detection limits were demonstrated but quantitative estimates could not be made.

2.3.2.3 Air Samples--

Samples collected on polystyrene membrane filters were dry ashed at 400 C and the resulting residues were dissolved in a mixture of acids in a Teflon bomb (Ranweiler and Moyers, 1974). In the multielement analysis of these solutions it was noticed that the lead blank for this membrane was higher than that found for cellulose filters.

A unique technique for separating and concentrating air particulates into two particle size ranges utilized a dichotomous sampler containing a virtual impactor (Dzubay and Stevens, 1973). The sizes that were separated included particles of less than and greater than 2 micrometers. An analysis of these fractions using X-ray fluorescense (XRF) revealed that lead is highly concentrated in the smaller sizes characteristic of emissions from auto exhausts.

Analysis of dustfall deposits on impervious Teflon discs is subject to less blank problems (Huntzicker, et al., 1975). Leachates of the discs were evaporated to dryness, redissolved and analyzed by atomic absorption. Dry ashing of glass filter catches produced lower extractions of lead due to the formation of insoluble silicate compounds (Kometani, et al., 1972). However, various ashing procedures for filter papers performed well.

2.3.2.4 Rock and Soil Samples--

In order to further identify lead species deposited in soils from auto exhaust systems, gradient density and magnetic separation methods were used to separate lead compounds for X-ray diffraction studies (Olson and Skogerboe, 1975). The lead compounds are concentrated in the high density fraction with the larger amount being present in the nonmagnetic aliquot.

Comparative leachings of soil were carried out using a mixture of sulfuric and hydrochloric acids and ammonium acetate. There was a considerable reduction in the lead extraction efficiency for the latter agent (Kahn, et al., 1972).

2.3.2.5 Miscellaneous Samples--

An automated procedure for determing lead in a large number of unleaded gasolines was reported using a two-reagent extraction scheme (Heistand and Shaner, 1974). Alcoholic iodine and dilute nitric acid solutions were used for the lead separations. The results were mainly within the allowable tolerance in comparison to the direct assay method (Annual Book of ASTM Standards, 1973).

Lead in oils has been determined using comparatively short (minutes) extraction of the lead additive and its subsequent estimation by titration (Banerjee and Dutta, 1973). The reagents used were thioglycollic and nitric acid.

Low-temperature (about 150 C) radio frequency ashing of coals was performed in an oxygen atmosphere to yield unaltered ash to concentrate lead and other metals for analysis by spectrographic methods (O'Gorman and Walker, 1972).

2.3.3 Methods of Analysis--

The forgoing information is only a partial summary of the research efforts which are being applied in the search for more rapid methods of pretreatment of environmental samples without sacrificing efficient recoveries of lead. The necessity of reliance upon sample treatment will become evident in the following comparisons of analytical methods available for determining lead at trace levels.

A comparatively large number of analytical methods are being used for trace lead analysis. Table 2.6 lists these methods along with the pertinent features and requirements to be met in the determination of lead for a variety of samples. Included for each method are the general pretreatments necessary for accomodation as to sample form and concentration. The other factors which describe the suitability of a method--detection limit, sensitivity, precision and accuracy--are reported from data found in the literature. Some workers use the terms sensitivity and detection limit interchangeably, so it is sometimes difficult to separate these parameters. Wherever possible, the sensitivity values listed represent those for which analyses can be made above the detection limit with reliability. The precision information is based on results obtained on replicate samples, and the accuracy assessment is based upon comparisons from the analyses of the same sample using at least two methods of analysis. These analytical limits can and will vary among analysts depending upon equipment, operation and diligence.

Table 2.6 ANALYTICAL METHODS FOR DETERMINING LEAD AT LOW LEVELS

Analytical Method	Required Sample Form	Important Applications	State of Measured Lead	Detection Limit for Lead
Colorimetric (dithizone)[a]	Liquid	Water and all other samples which can be chemically treated.	Lead dithizone complex	<1 ppm
Atomic absorption spectroscopy (flame)[b,k]	Liquid	All samples after chemical treatment.	Free atoms	30 ppb
Atomic absorption spectroscopy (flameless)[c,k]	Liquid or solid	All samples with varying degrees of pretreatment.	Free atoms	<1 ppb
Instrumental photon activation analysis[d]	Liquid or solid	All samples.	As is	12 ng/m^3 1.5 ppb (by volume)
X-ray fluorescence spectrometry[e,k]	Liquid or solid	All samples.	As is	1 ppm (10 ng/cm^2)
Spark source mass spectrometry[f,k]	Solid	All sample types with treatment.	Ions	<0.1 ppm
Electrochemical (anodic stripping voltammetry)[g,k]	Liquid	Water direct; other samples are converted.	Amalgams	0.5 ppb/ 5 ml
Atomic fluorescence spectrometry[h,k]	Liquid or solid	All samples with varying degrees of pretreatment.	Excited atom state	1 ppb (30 µl)
Optical emission spectrometry (arc source)[i,k]	Liquid or solid	All samples; some require treatment.	Vibrationally excited atoms	<1 ppm
Optical emission spectrometry (plasma source)[j]	Liquid	All samples which can be liquified.	Vibrationally excited atoms	2-8 ppb (100 µl)

Table 2.6 ANALYTICAL METHODS SUITABLE FOR DETERMINING LEAD AT LOW LEVELS (cont'd)

Analytical Method	Sample Preparation	Methodology	Interferences
Colorimetric (dithizone)[a]	Liquid is chelated with dithizone and the complex is extracted with an organic solvent. Double extraction at high pH may be needed to eliminate interference from other metals.	Absorbance of complex is determined spectrophotometrically at 510 nm.	Bi, Sn, and Fe in moderate amounts.
Atomic absorption spectroscopy (flame)[b,k]	Water samples may require concentration; biological samples, soils, and other solids are dissolved, chelated, and extracted.	Solution is nebulized and lead is atomized with a high temperature flame to produce free atoms which absorbs light of wavelength 283.3 nm.	Chemical and matrix effects must be overcome. Background may vary.
Atomic absorption spectroscopy (flameless)[c,k]	Water and biological fluids require little treatment. Solids may have to be digested and extracted.	Lead is atomized by thermal sources to provide absorbing free atoms.	Chemical and matrix effects overcome by proper standardization, must be aware of furnace emissions, nonreproducibility, and background problems.
Instrumental photon activation analysis[d]	Most samples can be irradiated directly. Radiochemical separations may be needed in some cases.	Samples are irradiated with optimum electron energies, and the resulting gamma rays are measured with a high resolution Ge(Li) detector. Interference-free 204 Pb line is used.	Overlapping of gamma ray peaks may require selection of less sensitive wavelength.
X-ray fluorescence spectrometry[e,k]	Filter catches can be analyzed directly; soils and biological samples should be dried, ground to at least 44µm, and pressed into pellets. Water samples require preconcentration by ion exchange or anodic stripping.	Samples are irradiated with primary source of X-rays to produce characteristic secondary X-rays for measurement by energy or wavelength dispersion.	Interelement effects, scattering from primary X-rays, overlapping peaks.

Table 2.6 ANALYTICAL METHODS SUITABLE FOR DETERMINING LEAD AT LOW LEVELS (cont'd)

Analytical Method	Sample Preparation	Methodology	Interferences
Spark source mass spectrometry[f,k]	Biological fluids are lyophilized, water samples are evaporated to dryness, filter catches and soils can be used without chemical treatment. All nonconductive samples require addition of graphite to form conductive electrodes.	Radio frequency spark is used to produce ions with the proper isotopic distribution for either photographic plate or electrical detection readout.	Organic matrix and complex ion formations, high background from major elements present.
Electrochemical (anodic stripping voltammetry)[g,k]	Water samples as is, solids and biological samples chemically treated to provide a liquid.	Electrolytic reduction of lead onto a Hg electrode followed by its determination using a reverse oxidation potential according to its standard electrode potential.	Possible peak potential overlaps, presence of organolead prevents total lead determination.
Atomic fluorescence spectrometry[h,k]	Biological fluids and water can be analyzed directly; other samples may require treatment for proper form.	Lead is atomized by a heat source and excited by a light source to fluoresce and emit characteristic radiation for measurement upon deactivation.	Chemical matrix effects and fluorescent quenching of desired radiation.
Optical emission spectrometry (arc source)[i,k]	Biological samples are dried or ashed and then arced. Water samples can be analyzed directly or via dried residue. Soils and air collections are arced directly.	Samples are arced in a pure graphite cup to produce spectral lines of the analyte. Readout of optimum lead line (213.3 nm) can be done by film or direct reader.	Spectral, chemical, and ionization effects can be overcome by simulation of standards makeup with matrix of samples.
Optical emission spectrometry (plasma source)[j]	Soils must be chemically converted to liquids; water and biological fluids can be aspirated directly or after slight dilution.	Sample solution is nebulized into a hot, inductively excited plasma of Argon gas to convert almost all of the analyte atoms to an excited state to provide the characteristic line spectra.	No chemical effects, Fe may interfere with lead analysis; background and instability should be controlled.

Table 2.6 ANALYTICAL METHODS SUITABLE FOR DETERMINING LEAD AT LOW LEVELS (cont'd)

Analytical Method	Sensitivity	Precision	Accuracy	Comments
Colorimetric (dithizone)[a]	--	20%	10%	Method is specific in absence of interfering metals.
Atomic absorption spectroscopy (flame)[b,k]	2.5 μg/1 for 1% absorbance	4%/25 μg/1	5%	Method is specific. Standards preparation must simulate sample matrix.
Atomic absorption spectroscopy (flameless)[c,k]	3×10^{-10}g per 1% absorbance (equivalent to air concentration of 0.1 μg/m^3	5-10%/10 μg/1	5-20%	Method is specific. Small (μl) volumes can be used. Short overall analysis time.
Instrumental photon activation analysis[d]	—	5-10%	10%	Specific, but equipment cost and time of analysis may be a disadvantage.
X-ray fluorescence spectrometry[e,k]	--	<5%	≤10%	Method is rapid, precise, and has multielement capability. Standardization can be a problem.
Spark source mass spectrometry[f,k]	—	±3x	>±3x (without standards) ±10-25% (with standards)	Good multielement coverage at low levels, isotopic dilution can provide accurate determination of trace metals.
Electrochemical (anodic stripping voltammetry)[g,k]	0.1 μg/1	2-6% 0.1 μg/1	10%/ 50 μg/1	Possibility of multielement (6) determinations, equipment simple but requires skill for operation, specific.

Table 2.6 ANALYTICAL METHODS SUITABLE FOR DETERMINING LEAD AT LOW LEVELS (cont'd)

Analytical Method	Sensitivity	Precision	Accuracy	Comments
Atomic fluorescence spectrometry[h,k]	3×10^{-11}g per 1% abs.	5%/0.1 µg/ml	--	Multielement capability; equipment commercially unavailable; light source problems include instability, nonreproducibility and operation. Aqueous standards can be used.
Optical emission spectrometry (arc source)[i,k]	1 ppm (25 mg sample)	13% 20-2000 ppm level	±20%	Fast, multielement analysis over a broad concentration range.
Optical emission spectrometry (plasma source)[j]	10 ppb	5% 1 ppm level	5%	Multielement analysis capability, a wide range of Pb content can be determined without the need for dilution, simple standards can be used.

[a] Lerner (1975).
[b] Edmunds et al.,(1973); Kinrade and Van Loon (1974); Amore (1974).
[c] Edmunds et al.,(1973); Anderson and Mesman (1973); Gross and Parkinson (1974).
[d] Aras et al.,(1973).
[e] Giauque et al.,(1973).
[f] Fitchett et al.,(1974).
[g] Ediger and Coleman (1973); Searle et al.,(1973).
[h] Browner (1974); Amos et al.,(1971); Winefordner and Elser (1971).
[i] Seeley et al.,(1972); Bedrosian et al.,(1968).
[j] Greenfield et al.,(1975).
[k] Coleman (1974).

The following sections describe the analytical methods which have been used in the overall analyses of lead in a variety of samples. Most recorded work deals with chemically-treated samples using one of the many techniques described earlier. Recent modifications and improvements in analysis methods and techniques have tended to require little or no chemical treatment of the sample, but in some of these cases reliability and general acceptance of the technique have been less than desirable.

2.3.3.1 Atomic Absorption Spectroscopy (AAS)--

This method is based upon the formation and the subsequent absorption properties of the atomic vapor of an analyte. The absorbance of a specific wavelength of light is measured which is characteristic of the element to be determined. For lead either 283.3 or 217nm can be used; the former is more commonly used. Several atomizing techniques can be used for converting the element sought into free atoms. These techniques provide varying degrees of conversion efficiencies and are generally dependent upon the atomizing temperatures attainable. These differences will be discussed below.

According to the literature, no method other than AAS has been as widely accepted and compared as a standard for trace lead analysis in the last five years. The advantages of low cost and ease of operation along with fulfilling conventional analytical criteria has contributed to the acceptance of this method. Improvements in atomization techniques during the last decade have extended the ability of atomic absorption spectroscopy to cope with the problem of choosing a compromise between reductions in required sample pretreatment and dependable results. The lowered detection limits and correspondingly more rapid sample preparation and analysis are seen to reflect these improvements. The atomizing capabilities presently available for AAS are the conventional flame, semiflameless and flameless. Maximization of sensitivities for each of these techniques can be achieved by adjusting the various operational parameters (Hwang, et al., 1972).

The conventional flame technique of AAS requires liquid samples for nebulization into air-acetylene or nitrous oxide-acetylene flame where atomization of the analyte occurs. The concentration is determined by measuring the absorption effects on a spectral source comprised of the same element. Analyses are carried out with an analyte concentration around 0.5-1 ppm or above. Therefore, chemical treatment is generally a prerequisite for achieving both the proper sample form and concentration range.

When analyzing plant samples by AAS, De Vries, et al., (1975) encountered difficulties of a kind likely to be encountered with other biological samples. Solutions of dry-ashed samples gave spurious results due to salt effects, which appeared to be additive. In addition, recoveries of lead from dry-ashed samples were generally low when compared with wet-ashed samples, due to partial volatilization of metal salts, to fixation in an acid-insoluble residue, or both. Wet-ashing eliminated this problem but it was found necessary to extract the sample into an organic solvent before analysis to attain the desired sensitivity and to remove interferences. Samples were decomposed with a nitric acid-perchloric acid mixture, diluted, buffered with citric acid and extracted with APDC-MIBK for analysis. Small amounts of iron in the standards and unknowns increased the stability of the solution and reproducibility of the analysis.

A technique has been described by Hessel (1968) for determining lead in blood erythrocytes using the flame source. Comparatively large volumes of blood are chelated and extracted for comparison with synthetic standards. The lead content in blood and urine samples is quite low. For blood analyses, 5 to 20 milliliters are often needed for adapting to the range of flame AAS. This involves continual withdrawal of large volumes of blood which is unattractive in clinical studies.

The disadvantages attendant to the use of flame techniques have resulted in the development of the more sensitive and rapid semiflameless and flameless approaches. The semiflameless techniques initially investigated for this purpose use tantalum boats (Kahn and Sebestyen, 1970) and nickel crucibles (Delves, 1970). With these modifications sensitivities are increased by at least a factor of 10 over the flame method. Both approaches utilize procedures of drying small quantities of samples in appropriate containers placed near the flame of a conventional AAS unit. After drying, the containers with their residues are inserted into the flame where temperatures are sufficiently high to vaporize and atomize the lead.

For analysis using the tantalum boat technique, volumes of less than 0.5 milliliter of blood or urine can be inserted directly, dried and measured for lead within several minutes. Previously analyzed samples (secondary standards) can be used for calibration. Reproducibility and comparison of these results with those of other methods are variable. This may be due to differences in tantalum boat positioning and to its deterioration.

The Delves technique requires addition of hydrogen peroxide to partially oxidize the blood sample (10 microliters), and overall, takes about 5 minutes for analysis. Standardization is accomplished by the standard additions procedure. Nonlinearity occurs at high lead levels thereby precluding the use of standard additions at these levels. However, reproducibility and comparison with other methods on similar samples are good. Evaluation of the Delves technique has been made by numerous investigators. Many hospitals have adopted the method after comparing results with those of several other methods (Hicks, et al., 1973; Marcus, et al., 1975).

Lead may be analyzed from small amounts of capillary blood specimens. Insufficient cleansing of the fingers prior to capillary sampling is a more likely source of possible contamination of capillary blood samples than of venous blood samples. Further simplification fo the Delves method is possible by the collection of capillary blood onto filter paper; after drying, small discs are punched out for insertion into the cup. Dispensing volume errors are eliminated using this approach (Cernik, 1973; Cooke, et al., 1974). This technique has also been used for the direct determination of lead in urine and was found to provide excellent results (Anderson and Mesman, 1973). Simultaneous background correction should be made for this and many other types of samples analyzed by atomic absorption.

The flameless technique provides high atomization temperature by resistance heating of a graphite furnace or carbon rod assembly. Sensitivities are increased by up to 3 orders of magnitude over the flame technique. However, the precision of analysis is much worse than for flame methods, typically 5 to 25 percent depending on the type of atomizer and type of sample (Coleman, 1974). The graphite atomizer allows the direct introduction of solid samples, but such samples are often lacking in reproducibility. The general procedure for analyzing small 10- to 50-microliter volumes of blood placed in the atomization cell is to dry at a low temperature (100 C), ash at a higher temperature (500 C), and then atomize at 2300 C (Fernandez, 1975). Background corrections are necessary. Also, synthetic aqueous standards can be used. Comparison with results obtained by the conventional extraction-flame technique are often favorable.

Slight changes in pretreatment procedures essentially eliminated the need for background corrections in the analysis of lead in blood using a graphite boat (Garnys and Matousek, 1975). After adding nitric acid, the results which were obtained showed excellent agreement with those determined by different procedures of chemical treatment and atomization. Sources of errors encountered in blood lead analysis using the graphite boat is the subject of a publication by Baily and Kilroe-Smith (1975).

Further information on other individual techniques of nonflame analysis of blood lead content is available. This includes the determination of lead in human erythrocytes using the graphite furnace (Evenson and Pendergast, 1974) and whole blood and plasma lead analyses using the carbon rod atomizer (Kubasik, et al., 1972; Matousek and Stevens, 1971).

Applications of flameless atomizers are being made for the analysis by AAS of particulate samples collected from ambient air. Although lead is generally present in urban air at or near 2 micrograms per cubic meter (often directly determinable by flame techniques), the direct analysis of particulates on filter media seems attractive. Sampling of small air volumes (100 to 500 cc) through high density graphite cups which are inserted directly into a graphite furnace provides rapid spot checks of atmospheric lead pollution. The sensitivity reported was in the 10^{-12} gram range (Woodriff and Lech, 1972). Standardization was made with aqueous solutions.

Monitoring of lead concentrations in air was performed by passing ambient air over inductively heated graphite rods for atomization and subsequent absorbance measurement (Robinson, 1973). Analytical sensitivities of 0.16 microgram per cubic meter were achieved.

Flameless and semiflameless atomic absorption can be used to determine lead in water withour preconcentration. Small volumes (microliters) of water can be analyzed. Errors in precision appear to be caused by inaccurate volume dispensing, deterioration of the tantalum boat or graphite furnace and by the possible instability of stored samples. The following articles relate these problems to the analysis of lead in water samples at low (ppb) concentrations (Ediger, et al., 1974; Fernandez and Manning, 1971; Edmunds, et al., 1973). A modification of the Delves cup technique was used successfully (Maines, et al., 1975) for lead analyses of potable waters. Microliters of water were introduced along with gelatin into the cups to yield results which were in excellent agreement with the solvent extraction-flame procedure.

Some form of preliminary chemical treatment of most biological materials other than blood is apparently necessary for analysis by flameless AAS. The fact that the detection limits are lower than in flame applications is an argument for their use even when such treatments are required.

Addition of graphite to pulverized rock samples enhanced the atomization of lead for direct measurements using an inductively heated graphite furnace. However, only moderately precise data were obtained when compared to X-ray fluorescence values (Langmyhr, et al., 1974).

2.3.3.2 Absorption Spectrophotometry--

The standard method of choice for years for the analysis of lead was the dithizone method. After chelation by dithizone (diphenylthiocarbazone) and extraction, the complex is analyzed by a spectrophotometric procedure based on the absorption of light at a particular wavelength. This method is widely used as a comparison for new techniques and methods (Weiss, 1972; Annual Book of ASTM Standards, 1972). The method is sensitive to lead at the microgram level. Preconcentration treatments are required prior to using this method for lead assay. As with all concentration and separation procedures, extreme care should be excercised for efficient recovery of lead and the elimination of other metallic interferences. The method can be precise and specific.

A variation of the dithizone method is the ring-oven technique which was used to determine lead in ambient air particulate samples at microgram levels (Shendrikar and West, 1972). The method involves the diffusion and concentration of lead dithizonate into narrow zones on filter paper for its estimation from comparisons with similarly prepared standards. Reasonable agreements with AAS methods were achieved. This method may be useful for field monitoring of the lead content of air.

2.3.3.3 Electrochemical Techniques--

Advanced polarographic techniques have aroused increasing interest in their use as an analytical tool capable of precise trace metal analysis. The reader is referred to a review of these improvements in polarography in its competitive application to environmental samples (Flato, 1972). The electrochemical characteristics of lead are very favorable.

Various procedures are described below for the analyses of low lead concentrations in liquids or acid digests of solids. Pulsed voltammetric stripping (PVS) was used to determine lead in the low ppb range in water, urine, blood plasma and digested whole blood (Copeland, et al., 1973). Very good agreement was found between results of this method and those obtained using nonflame AAS. Analytical conditions were optimized (Hg film in place of a drop) to attain higher sensitivities. Using linear scan anodic stripping voltammetry (ASV), investigators determined the lead content of chemically-treated blood and urine samples. The results agreed well with those obtained by flame AAS (Searle, et al., 1973).

Other electrochemical techniques which may be used in the direct analysis of lead in water in the ppb range are pulsed ASV (Crosmun and Dean, 1975); cathodic SV (Kinard and Propst, 1974); and alternating current ASV (Rojahn, 1972).

The electrochemical methods are specific for lead and usually provide a means of multielemental analysis.

2.3.3.4 X-ray Fluorescense (XRF)--

XRF can be used for determining micro and trace quantities of lead in a wide variety of samples. Ambient air filter samples can be measured directly with the quality of the results being dependent upon suitable standardization, particle size and interelemental matrix interferences (Lee, et al., 1972). The latter may be reduced with proper standardization or the use of mathematical relationships for corrective purposes. Unless present in sufficiently high quantities, lead in water is best analyzed after concentration on ion exchange membranes (Campbell, et al., 1966). Some biological materials (freeze-dried) can be analyzed directly for semiquantitative data in the absence of simulated standards (Giauque, et al., 1973).

Energy dispersive readout of XRF was used to measure microgram quantities of lead in biological, rock, and air samples (Giaugue, et al., 1973). The biological specimens were freeze-dried and pressed into thin wafers before irradation with primary X-rays from a Mo target. Rocks were finely ground and redispersed onto suitable membranes prior to measurement. Ambient air particulates were analyzed directly on filters.

Gamma-ray excitation is used in a portable lead detector for screening painted walls for potential lead ingestion sources (Laurer, et al., 1971).

Proton-induced X-ray emission analysis (PIXEA) using an energy-dispersive readout was investigated for lead determinations in a variety of environmental samples (Walter, et al., 1974; and Lochmuller, et al., 1974). The use of proton excitation reduces the white radiation background and increases X-ray excitation to provide greater sensitivities. The former investigators determined lead in soil extracts, in leaf sections, dried body fluids, air catches, thin tissue sections and proteins by direct measurement. Difficulties were experienced in achieving quantitative results and suitable sensitivities.

The combination of a primary source for sample irradiation and wavelength dispersion was used to quantitatively determine lead in gasoline (von Lehmden, et al., 1974).

2.3.3.5 Activation Analysis--

Environmental samples analyzed for lead by this method are better treated by radiation sources other than neutrons. The low nuclear cross section of lead and intereferences associated with neutron activation reduce the sensitivity for lead considerably beyond that required for meaningful analysis in many cases. Other forms of irradiation induce more sensitive lead reactions so that lead can be determined in trace quantities in all forms of samples. In conjunction with instrumental attachments, greater sensitivities can be obtained.

Photon irradiation (2 hours) performed directly on atmospheric (Aras, et al., 1973) and soil (Chattopadhyay and Jervis, 1974) samples allowed the determination of lead at accuracies competitive with other methods of analyses. Irradiation of air particulates for one hour with ^{3}He ions permitted the measurement of the product Po^{207}, representing converted lead at low levels (Parsa and Markowitz, 1974). Good precision was observed at microgram per cubic meter levels.

2.3.3.6 Spectrographic Methods--

The methods described in this section include mass and optical spectroscopy. Various sources for excitation or ionization are available for spectrographic measurements, but only a few will be covered.

Emission spectroscopy has been a standard qualitative and semi-quantitative laboratory tool for years. Samples are deposited on graphite or metal electrodes and excited to produce spectra characteristic of the element. Comparison of the spectra of known and unknown compounds provides qualitative identification of the elements in the sample; if standards are used for the known samples, semiquantitative and quantitative analysis is possible. Seeley, et al., (1972) compared emission spectrography and AAS for the determination of lead transported to soils from automobile exhausts. Soils were analyzed for lead by direct arcing in graphite cups. Comparisons with digested samples analyzed by AAS agreed within 10 percent.

The combination of an inductively-coupled, plasma excitation source with optical emission spectroscopy (ICP-OES) has been used to achieve extremely high atomization temperatures for detection of lead at low nanogram levels. A small volume of liquid sample is introduced into an argon plasma where excitation of the free atoms occurs for their measurement. Attributes of ICP-OES are compared with those of other methods (Fassel and Kniseley, 1974) along with its use for the analysis of lead in a variety of samples (Greenfield, et al., 1975).

Spark source mass spectrometry (SSMS) is a highly sensitive analytical technique. The sample is vaporized by a radio-frequency spark and the resultant ions are spectrometrically measured according to their mass. Precision can be improved through the use of an isotopic dilution technique. Spark source mass spectrometry has been used for the analysis of biological specimens for heavy metals including lead (Fitchett, et al., 1974). The samples were dried and combined with conductive graphite to aid in sparking. Although detection limits for lead were in the ppb range, the organic content interference required proper graphite dilution ratios.

2.3.3.7 Atomic Fluorescence Spectroscopy (AFS)--

Compared to its related counterpart (AAS), AFS has not enjoyed the extent of application to trace metal analysis. Both techniques show similar sensitivities for lead determinations. Since AFS equipment is not generally commercially available, modification of existing AAS equipment is required for its use. The reader is referred to publications outlining the potential of AFS (Browner, 1974; Winefordner and Elser, 1971). Lead has been determined in blood and urine using the flameless carbon rod atomizer (Amos, et al., 1971). Although lead levels determined were comparable to nonflame AAS values, considerable experimental difficulties were experienced. This method appears to be in the developmental stages, with its potential not yet fully developed.

2.3.3.8 Biological Methods For Determining Body Lead Exposure--

Considerable efforts are being made to develop analytical procedures suitable for diagnostic use on persons suspected or known to have elevated lead exposure. The effect of excessive lead on metabolism is reflected in its inhibition of enzymes required in heme synthesis. The protoporphyrin IX content of blood which reflects inhibition of heme synthesis in bone marrow can be determined with relative ease on microcapillary samples (Sassa, et al., 1973). Two milliliters of whole blood provide a sufficient sample to determine the separated porphyrin content fluorimetrically. This method and minor modifications developed by others are somewhat non-specific. Porphyrins other than protoporphyrin IX register fluorescence under the conditions of porphyrin extractions used. This is not a major problem since other porphyrins are elevated only in the case of the relatively rare porphyrin disease, e.g. erthrocytic protoporphyria. Nevertheless, in recognition of this non-specificity, the results are expressed as micrograms of "free" erthrocyte porphyrin (FEP) rather than as units of protoporphyrin. Log FEP has been found to rise linearly with blood lead concentration in adults (Haeger-Aronson, 1971) and children (Piomelli, 1973; Sassa, et al., 1973).

Lamola and Yamane (1974) found that the fluorescent porphyrin in the erythrocytes of patients with lead intoxication or with iron deficiency anemia is zinc protoporphyrin which is bound to globin moieties, probably at heme binding sites. Measurement of the fluorescence at 594 nanometers of blood directly (without any extraction steps) can serve as a simple screening test for lead intoxication. Experimental procedures developed by Lamola, et al., (1975) have confirmed the simplicity and rapidity of the method. Small capillary quantities of blood are diluted prior to measurement of their fluorescence. This metabolite is stable in properly stored blood.

The measurement of coproporphyrin in the urine has long been used as an index of excessive lead exposure in industry. Coproporphyrin is first extracted from the urine into either ethylacetate-acetic acid (Sano and Rimington, 1963) or into diethyl ether (Askevold, 1951). Absorbance is then measured at 401 nm. The methods are apparently specific since uroporphyrin, the only likely source of interference, is not extracted under the conditions described above (Rimington and Sveinsson, 1950).

The rate of urinary excretion of delta-aminolevulinic acid (ALA) also has been used as an index of excessive lead exposure. The basic procedure commonly used today was originally reported by Mauzerall and Granick (1956). The method and subsequent modifications thereof depend on the formation of a colored complex of pyrrole derivative of ALA with p-dimethylaminobenzaldehyde (DMAB). The method is non-specific. DMAB forms colored complexes with many pyrroles formed by Knorr condensation of aminoketones other than ALA, notably aminoacetone (AA), which occurs in biological fluids. Modifications of the method of Mauzerall and Granick separate AA from ALA prior to coupling with DMAB (Urata and Granick, 1963; Marver, et al., 1966). Like all enzymatic methods, ALAD activity is dependent on such variables as pH and temperature of the enzyme-substrate preparation. Numerous specific assay procedures have been used, all of which vary in such specific details (see, for example, Nikkanen, et al., 1972; Bonsignore, et al., 1965; Tomokuni and Ogata, 1972).

2.3.4 Comparison of Analytical Methods

The applicability of an analytical method for determining lead in environmental samples depends on the intended use of the results. As this relates to health effects brought on by excessive lead exposures, it is imperative that the methods provide the results rapidly and with accuracy as well as precision so that treatment can be given to alleviate the condition. Conversely, for studies involving lead in relation to source, emission routes, fate, chemical form, elemental associations and mass balance, a fast analytical response is not required. To some extent these studies may also include the measurement of other trace metals present along with lead. Therefore, the need of the investigator for simultaneous multielement analyses will also dictate the method of choice.

The colorimetric dithizone method is still considered by many laboratories as their adopted or backup method for determining lead in samples which have been chemically treated. By taking the necessary precautions to eliminate interferences and insure complete recovery of lead as a complex during sample preparation, this method is competitive with the more recently emphasized techniques. In general, the method is reliable and where time is not a consideration, it can be used with confidence.

Atomic absorption spectroscopy compares very favorably with both the established and the new methods of analysis. It possesses the features which are desirable for an analytical method: specificity, low limit of detection, accuracy, fast turn around time and comparative ease of operation. Although capable of analyzing up to 60 elements, sequential, rather than simultaneous, multielemental analyses are possible with the same sample solution. The flame atomizer requires, in most cases, some form of sample treatment to obtain the proper sample concentration and form. The flameless atomizer modifications have, to some extent, eliminated the need for extensive pretreatment for some samples. Projected use and continued exploration of this atomizing technique will undoubtedly result in the direct, or with slight modification, insertion of other environmental samples of interest. Present operational and stability problems of the latter atomizing technique are also expected to be corrected with this increased emphasis. The widespread use of AAS for determining lead and other metals at trace levels is an indication of its acceptance for reliability of analysis. Atomic fluorescence, like atomic absorption, is capable of multielement analysis, but this capability has not been commercially developed.

Optical emission spectometry (OES) techniques provide analyses which encompass wide elemental and concentration ranges in the proper sample form and are particularly suited to multielement analyses. The arc source OES is suitable for the direct analysis of soils and dried tissues and also for solutions which contain lead in the microgram range. The inductively coupled plasma source of OES has great potential as a future method for rapidly determining lead and other metals at the nanogram level in solution samples. The forte of these OES techniques is in obtaining rapid survey characterization of samples requiring elemental associations and base-line studies.

The electrochemical methods require comparatively simple equipment with excellent sensitivity for lead in the analysis of liquid samples. Multielemental analysis is possible although the number of elements determinable is limited. The increased sensitivities gained from the various modifications of polarography and anodic stripping make them well suited for determining lead at the nanogram level. The precision and accuracy derived from these techniques compared favorably with AAS.

Spark source mass spectrometry (SSMS) can be used for the direct analysis of a variety of sample types. Semiquantitative information can be generated at the sub-ppm level for most of the elements, including lead, without standardization. The high cost of equipment, the level of operator expertise required and other attendant difficulties limit the use of SSMS for single element analysis. Its use for multielement determinations can be very advantageous.

X-ray fluorescence can be used for the direct analysis of soils and atmospheric filter catches and concentrates or residues of aqueous solutions. Standardization is a problem in heterogeneous samples although the contents of lead among samples can be determined with a reasonable level of accuracy relative to each other. This method can also be used to determine lead in liquid fuels with a greater degree of accuracy than that obtained with other samples because of the ease of standard preparation. The simultaneous, multielement capability is available when using energy or wavelength dispersive readout techniques.

Proton or photon activation analysis offer the advantage of being able to analyze for lead with little or no sample preparation. As with SSMS, equipment availability and time of analysis preclude its wide use except in rare situations.

2.3.4.1 Standards and Standardization--

An accurate assessment of trace levels of lead in environmental samples necessitates the use of methods of analysis which permit comparison. The low concentrations of lead which are encountered preclude the use of absolute gravimetric methods. Standards can be classified as primary (certified), secondary (previously analyzed), and synthetic (laboratory prepared).

Table 2.7 lists the National Bureau of Standards (NBS) standards of significance to lead environmental studies which are presently available. The range of lead concentrations offered in the liquid fuels allows working curves to be obtained for accurate determinations of lead. The single-value lead standards available for the other sample types can provide a good check on chemical treatment recoveries and the evaluation of analytical procedures.

Table 2.7 AVAILABLE NBS PRIMARY SAMPLES FOR LEAD
IN VARIOUS ENVIRONMENTAL SAMPLES[a]

Sample	SRM No.	Pb Content
Orchard leaves	1571	45. ppm
Bovine liver	1577	0.34 ppm
Paint	1579	11.87%
Coal	1632	30. ppm
Coal fly ash	1633	70. ppm
Fuel oil	1634	(Pending Certification)
Liquid fuels	1636	12, 20, 28, 773 μg/g
	1637	12, 20, 28 μg/g
	1638	773 μg/g

[a] Adapted from Catalog of NBS Standard Reference Materials, NBS Special Publication No. 260, 1975-76.

Other standards are available, e.g., U. S. Environmental Protection Agency water samples, and U. S. Geological Survey rock samples.

Secondary standards can be used when available and when appropriate. Previously analyzed blood samples have been used successfully with the flameless techniques of AAS for calibration purposes. Preservation may be a problem with their use over extended periods of time. Secondary standards possessing an adequate concentration range of the analyte can be used as standards in the direct analysis of fuels and air particulate catches by many techniques. Careful storage of these standards will insure their stability for long periods.

Chemical treatment of the samples provides an added advantage in that appropriate similar aqueous standards can be prepared to more closely resemble the chemical makeup of the concentrate. Simulation of the sample matrix with the standard compensates for interferences in many instances.

For AAS applications, standards with simulated matrices can be used separately, for comparison, or may be incorporated into the sample by employing the method of additions technique. The latter technique is used to compensate for interference effects. It does not accomplish this in every case, however. Some indication of the variation in the results obtained with standards used in the Delves cup procedure of determining lead in blood is provided by a study, in which Olsen and Jatlow (1972) compared and related the addition of synthetic standards in several matrices and cup treatments. They found that the direct use of aqueous standards was successful if the nickel cups were first treated with albumin. This modification eliminated the need for using the method of additions which required more analyses per sample.

Synthetic aqueous standards can be used directly for optical emission spectroscopy with an inductively-coupled plasma as the atomizing source. Because of the high temperatures attained using this source, most interelement or matrix problems associated with other atomizing techniques are considerably reduced. Both the direct method and the method of additions can be used for the application of solution standards in polarographic analyses with comparable success. Synthetic standards in solid forms can be prepared for use in both mass and X-ray spectrometry.

2.3.4.2 Interlaboratory Comparisons--

The constant desire and need for upgrading the results of determinations of metals at trace levels has produced rapidly improving modifications of existing preparation techniques and analytical methods. These improvements not only provide increased method sensitivities, but an awareness of the pitfalls of sample contamination during its preparation for analysis. One of the important activities in establishing the validity as well as the problem areas of an analytical method is interlaboratory comparison. Such cooperative studies provide useful information on sample preparation techniques as well as providing direct comparisons of the methods in relation to their applicability and the validity of results obtained. The results of most round robin comparisons have pointed out the difficulties of and the need for better approaches to trace metal analysis. The analysis of lead at trace concentrations, particularly in biological specimens, is no exception. Fortunately, more awareness of the problems associated with microanalytical techniques is being shown today. The results of past interlaboratory comparisons for a variety of samples containing lead at low concentrations are reported in the following paragraphs.

2.3.3.2.1 Biological samples--A number of interlaboratory programs have been conducted on the analysis of blood and urine for lead. Round robin analyses of blood samples have been shown to produce varied results (Keppler, et al., 1970). In one interlaboratory effort to compare blood analyses involving over 60 laboratories nearly one-half reported unacceptable data. Each laboratory used its preferred laboratory method and seven different methods were represented in this study. Not unexpectedly, it was reported that the laboratories were better able to determine the relative differences between samples than accurately measure the actual quantities present. No one method was totally acceptable. The poor results were evidently caused by a number of reasons; the stipulation of which can only be speculative.

In another comparison seven laboratories were asked to analyze one blood sample of known lead content (Donovan, et al., 1971). The lead was double extracted. In most cases, the dithizone method of analysis was used. The dispensing laboratory analyzed the pooled stock eleven times during a 3-month period to assure its stability. The results of the laboratories ranged from 10 to 150 micrograms per 100 grams of blood; the mean value obtained by the referee laboratory was 155 micrograms. Only 3 laboratories were within 3 sigma of the mean value obtained by the referee laboratory. There was no correlation between previous laboratory experience in blood lead analysis with the reliability of results. In the same study, 20 laboratories took part in the analysis of one urine sample for lead; only three reported results which fell within 3 sigma of the mean value reported by the referee laboratory.

Twenty-two laboratories analyzed one aqueous, spiked solution of lead and three different stabilized blood samples of unknown lead content (Berlin, et al., 1973). The majority of the participants, after the extractive procedures, used either AAS or the standard dithizone color method. On the spiked sample, 70 percent of the laboratories were within 10 percent of the added amount of lead. The results of the blood samples, however, showed a large range in each case with the greatest disparity being evident for the samples containing the lowest amounts of lead. It was suggested that contamination could occur in any phase of the procedure and was the cause of the spread obtained. As a result of that study, it was deduced that these procedures were too imprecise to measure small lead uptakes.

Three experienced laboratories engaged in an analytical comparison of lead in blood samples in 1973, and again in 1974 (Browne, et al., 1974). Two laboratories used AAS and one, anodic stripping. At the 95 percent confidence level, the mean difference between any two laboratories showing the greatest variation was plus or minus 29 micrograms per 100 grams in 1973 and plus or minus 44 micrograms per 100 grams in 1974. In both years, one out of three laboratories (not the same one) reported unacceptable data.

An extensive European, 66-laboratory program for the analysis of lead in blood and urine was undertaken (Lauwerys, et al., 1975). The program was designed to evaluate experience, analytical method and the precision of analysis. Extreme care was taken in sampling, homogenizing and stabilizing the pooled samples. The methods used for the lead analyses were primarily AAS (flame and nonflame) and colorimetric dithizone. Samples consisted of 3 blood, 2 urine and 2 aqueous, spiked samples and were run in triplicate. The overall range of reported lead contents varied as much as 2 orders of magnitude, with inter- and intralaboratory coefficients of variation of 50 and 10 percent, respectively. Experience and method of analysis did not appear to be a factor in the variation of results. The discrepancies were attributed to the systematic errors peculiar to each lab which may have arisen in their pretreatment, standardization, or analysis techniques.

Twenty-six laboratories reported on the analysis of six samples of urine containing various amounts of ALA, using three different techniques (Berlin, et al., 1974). A considerable range of ALA levels was reported on the urine samples taken from an unexposed subject; however, a better correlation was observed for samples containing higher amounts of ALA. The conclusion was that these procedures were not sufficiently precise to be relied upon in the determination of small differences in ALA.

The ALAD content in blood was analyzed in the cooperative effort of nine laboratories (Berlin, et al., 1973). Using variations of the classical method of Bonsignore (1965), reasonable agreements were obtained in the ratios of enzymatic activities found in two blood samples. Standards were not prepared for concentration estimates.

The difficulties and discrepancies in the analysis of lead in blood, as indicated by numerous interlaboratory comparison studies, are such as to suggest that (1) much more effort is needed to resolve these analytical problems; and (2) doubts are introduced into the validity of past analytical data upon which rests the understanding of the relationship between blood and lead.

While the above perhaps is not as disruptive as the discovery of the importance of alkyl mercury compounds in understanding and interpreting the environmental effects of mercury, it still points up a need for further research on the preparation and analysis of blood for trace levels of lead.

2.3.3.2.2 Foods--The lead content of four general food types was determined in a collaborative study involving eight laboratories. The study included specific procedures of chemical treatment and the proposed AOAC atomic absorption analytical method (Hoover, et al., 1969; Hoover, 1972). The coefficient of variation was no greater than 10 percent and much less in most cases. General indications are that this overall procedure is reliable and can be used for the determination of lead in foodstuffs. Lead is generally present in foods at levels below 1 ppm (see Section 8.3.1).

Eleven laboratories engaged in a round robin analysis of lead in evaporated milk (Fiorini, et al., 1973). The stipulated overall analytical procedure included dry ashing, chelation and extraction and analysis by either AAS or anodic stripping. Lead was found to be present in evaporated milk at the fractional ppm level. The coefficients of variation of the results at levels of 0.06 and 0.22 ppm were 43 and 4 percent for AAS and 28 and 6 percent for anodic stripping, respectively. The AAS method was chosen as the official first action by the AOAC because of the better agreement among the laboratories using this method.

Lead in fish was the subject of an effort of 19 laboratores (Gajan and Larry, 1972). The fish, generally containing lead at the less than 1 ppm level, were dry ashed at 500 C and dissolved in HCl. Lead was determined by AAS or polarography. Preliminary acquaintance with the procedural steps was achieved by attaining 90 percent lead recoveries on spiked fish samples. The results of this study indicate that the recoveries as measured by the two analytical methods were unusually efficient. The coefficient of variation for the polarographic and AAS results were reported to be about 8 and 13 percent, respectively. The polarographic method was chosen as the official first action by the AOAC because of the lower blanks obtained; however, either method can be used to check the other.

Sixteen laboratories took part in a cooperative effort to determine lead in apples at the less than 1 ppm level (Markus, 1974). The recoveries were quantitative within experimental error and the coefficient of variation for the between-laboratory comparisons was less than 5 percent after certain procedural changes were made to lower the high blanks obtained in an initial study.

2.3.3.2.3 Environmental samples--The analysis of lead in seawater was performed by seven laboratores (Patterson, 1974). Although the methods used for these analyses (atomic absorption spectroscopy and anodic stripping voltammetry) were subject to accuracy difficulties, efforts are being made to improve the use of these methods in regard to reducing blanks and increasing the amount of lead available for analysis. The deep water lead content as indicated by isotope dilution mass spectrometry measurement may have been in the low nanogram per kilogram of water range. This value disputes earlier investigators who reported this level to be in the microgram range. The previously high lead results for seawater were attributed to inadequate care in sampling and storage.

In another interlaboratory comparison of the analysis of ambient air for lead (U. S. Department of Health, Education and Welfare, 1965) using the standard dithizone method, a 30 percent difference in results from various laboratories for comparatively high concentrations of lead.

2.3.3.2.3 Fuels and emission products--Attempts were made to select the optimum analytical method for the multielement analyses of fuels and associated by products (von Lehmden, et al., 1974). Nine laboratories were asked to analyze as many as 28 elements in coal, fly ash, fuel oil and gasoline. Lead was one of the elements to be analyzed. The methods used for these analyses included NAA, AAS, SSMS, OES, ASV and XRF. The wide range of lead content (at the ppm level) reported by the various laboratories indicated that the use of different sample treatments and analytical methods can produce errors in the results. Reference materials are needed for determining recovery efficiencies. It was also determned that variations for some elements in certain samples was due largely to sample heterogenity. The results of these types of studies clearly emphasize the need for reference materials of an environmental nature. Without such materials, it will continue to be difficult to pinpoint sources of error for the various analysis methods and techniques.

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3.0 EFFECTS ON MICROORGANISMS

3.1 SUMMARY

Evidence was presented that indicates that bacteria in anaerobic lake sediments or incubated aquarium water can convert organic lead compounds into volatile lead. The chemical mechanism in the formation of tetramethyllead from trimethyllead acetate or lead acetate was not determined.

Inorganic lead was absorbed from culture media by bacteria and was found to be associated with their cell membranes. The lipids associated with bacterial cell membranes appeared to play a role in the nucleation of lead that resulted in lead inclusion bodies.

Inorganic lead (as lead salts or free ions) can inhibit bacterial growth, cell viability, and enzyme activities, and some phases of lipid biosynthesis.

3.2 TRANSFORMATIONS AND METABOLISM

Only the bacteria will be discussed in this chapter. No references on lead and viruses were found in the sources searched. For discussions of other organisms sometimes considered as microorganisms, see the following sections: algae and fungi (Section 4.2); zooplankton (Section 5.2); phytoplankton (Section 4.2) and protozoa (Section 5.2).

3.2.1 Biotransformations

Wong, et al., (1975) and Schmidt and Huber (1976) present evidence that microorganisms (bacteria) convert organic lead compounds into volatile lead (Table 3.1). Biologically active lake sediments and seeded aquarium waters yielded tetramethyllead from trimethyllead acetate (Wong, et al., 1975) and lead acetate (Schmidt and Huber, 1976), respectively. Pure cultures of *Pseudomonas*, *Alcaligenes*, *Acinetobacter*, *Flavobacterium*, or *Aeromonas*, in lake water or nutrient medium with or without sediment (Wong, et al., 1975) and light also produced tetramethyllead from trimethyllead acetate. None of the above biological seeds, however, had definite effects on the production of tetramethyllead from inorganic lead (Table 3.1). The mechanisms by which Pb^{++} is converted to tetramethyllead through microbiological activities still have to be investigated. Doubt has been cast on the significance of microbiological conversion of specific organic lead compounds to tetramethyllead because of the failure of bacteria to convert inorganic lead compounds (Table 3.1).

Jarvie, et al., (1975) suggest that a possible chemical mechanism for the formation of tetramethyllead from trimethyllead acetate in active, anaerobic sediment systems is the intermediate formation of trimethyllead sulfide

TABLE 3.1 MICROBIAL METHYLATION OF LEAD COMPOUNDS[a]

Pb Salt Added	Pb^{2+} Conc., µg/ml	Microbial System[c]	Incubation Time, Weeks	Volatile Me_4Pb Produced, µg	Reference
$Pb(NO_3)_2$	5	Lake sediment	2	--	Wong et al, (1975)
$PbCl_2$	5	Lake sediment	2	--	Wong et al, (1975)
$Pb(OH)_2$	5	Lake sediment	2	--	Wong et al, (1975)
$Pb(CN)_2$	5	Lake sediment	2	--	Wong et al, (1975)
PbO_2	5	Lake sediment	2	--	Wong et al, (1975)
$PbBr_2$	5	Lake sediment	2	--	Wong et al, (1975)
$C_{16}H_{32}O_2$-Pb	5	Lake sediment	2	--	Wong et al, (1975)
Me_3PbOAc[b]	10	Lake sediment	1;2;3;4	124;642[d] 550;256	Wong et al, (1975)
$Pb(OAc)_2$	1	Incubated aquarium water	1;2	106;103[e]	Schmidt and Huber (1976)

[a] Adapted from Wong et al, (1975) and Schmidt and Huber (1976).

[b] Trimethyllead acetate.

[c] Apparently pure cultures Pseudomonas, Acaligenes, Acinetobacter, Flavobacterium, or Aeromonas were also tested with each Pb salt with same results reported with the exception of incubated aquarium water.

[d] Reported as tetramethyl lead (Me_4Pb) produced at 1 to 4 weeks, respectively.

[e] Maximum amounts of volatile Pb produced; calculated as equivalent to Me_4Pb at 1 and 2 weeks respectively.

followed by decomposition to give tetramethyllead. In anaerobic conditions, this mechanism seems to be dominant in the formation of tetraethyllead from triethyllead chloride. The authors envisage that trialkyllead salts compete with inorganic sulfides to obtain the necessary sulfur. However, Schmidt and Huber (1976) point out the probability that lead sulfide is precipitated out of solution and that not enough lead may be in solution to allow appreciable alkylation to tetramethyllead.

3.2.2 Uptake and Absorption

Micrococcus luteus and *Azotobacter* sp. are highly capable of absorbing substantial quantities of inorganic lead (Tornabene and Edwards, 1972). *M. luteus* and *Azotobacter* sp. were found to concentrate 490 and 310 milligrams of lead per gram of whole cells (dry-weight basis), respectively, from culture media containing 2.5 mg $PbBr_2$/ml. The cellular lead was largely associated with the cell wall plus membranes with very little associated with the cytoplasmic fractions. The residual lead in the cellular membranes of *Micrococcus* and *Azotobacter* accounted for 89.8 and 61.5 percent of the total cellular lead, respectively. When Tornabene and Edwards (1973) exposed *M. luteus* to lead chloride and lead bromide for 20 consecutive days, the greatest portion of the cellularly-assimilated lead remained associated with the cell membranes.

Tornabene and Peterson (1975) found that individual lipids in the cellular membranes of bacteria, especially *M. luteus*, do not provide specific stable binding sites for lead. However, natural membrane lipid mixtures seem to have a role in the nucleation of lead (i.e., the formation of lead inclusion bodies) and consequently providing a possible vehicle for the transport of lead. Microscopic examinations of control and lead-treated *M. luteus* cells supported the *in vitro* studies by revealing electron dense inclusion bodies in membrane fragments in only the lead-treated cells (Peterson, et al., 1975).

No further references to lead uptake by bacteria were found in the sources searched.

3.3 EFFECTS

McConn, et al., (1967) have shown that the *Bacillus subtilis* neutral protease (bound to a zinc atom) is inhibited by an excess of Hg^{++}, Cd^{++}, Pb^{++}, and Ni^{++}. The zinc in the native enzyme is readily exchanged with Hg^{++}, Cd^{++}, Pb^{++}, and $^{65}Zn^{++}$ to form active compounds as demonstrated by their ability to hydrolyze the synthetic substrate hippuryl L-leucinamide.

In experiments to qualitatively test the possible inhibitory effects of heavy metals on a glutaminase isolated from *Escherichia coli*, Hartman (1968) incubated metal ions with the enzyme for 5 minutes at 25 degrees prior to adding glutamine. Glutaminase was inhibited 57 percent by one (1) millimole Pb^{++} (as lead acetate) and 100 percent by 0.1 millimole Hg^{++} (as mercuric nitrate). Cd^{++} (as cadmium acetate) was without effect at one (1) millimole.

Lead (10^{-4} M lead acetate) inhibits the incorporation of ^{14}C-leucine into *E. coli* t-RNA (Ulmer and Vallee, 1969). The authors indicate that this inhibition is due to the interaction of lead with the enzyme aminoacyl synthetase and the hydrolysis of leucyl t-RNA (see Figure 3.1). These experiments suggest that lead might affect protein synthesis both by attacking the synthesizing enzymes and bringing about the hydrolysis of t-RNA and, presumably, similar RNA species.

Inorganic lead inhibits the growth of the bacterium Rhodopseudomonas spheroides, and appears to alter tetrapyrrole synthesis in this species through a complex metal-ion antagonism involving coproporphyrinogen oxidase (coprogenase) (see Figures 3.2 to 3.5 and Table 3.2). Through these studies were derived the basis for the increased urinary coproporphyrin observed in plumbism (Ulmer and Vallee, 1969).

Devigne (1968b) observed stimulated growth of Sarcina flava in medium containing relatively high concentrations of Pb^{++}. This was accompanied by an increase in peptone degradation and in a number of biosynthetic reactions with PbS appearing as the final metabolite. Using a telluric Micrococcus, similar experimental results were obtained by Devigne (1968a). Growth of wild and recombination-deficient strains of Bacillus subtilis was equally inhibited by 0.5 M lead acetate and lead chloride in a rec-assay (method for screening chemical mutagens) of fifty-six metal compounds. No evidence of mutagenic activity was found for the lead compounds (Nishioka, 1975).

Sadler and Trudinger (1973), in a study of the inhibition of microorganisms by heavy metals, concluded that for E. coli the order of decreasing toxicity is: mercury, cadmium, lead, ferrous iron, copper, zinc.

According to Tornabene and Edwards (1972), lead bromide, lead iodide, and lead bromochloride in concentrations approaching solubility limits had no detectable effects on the overall growth rate and cell viability of Azotobacter sp. and M. luteus. Tornabene and Edwards (1973), however, observed that in the course of exposing Micrococcus luteus cells to lead (as lead bromide and lead chloride) for 20 consecutive days, osmotically sensitive cells resulted. These cells exhibited a loss of carotenoids but without any effect on the Vitamin K content of the cells. Peterson, et al., (1975) later demonstrated that M. luteus cells exhibited a sequence of changes in the quantity of total cellular lipids with essentially no changes from normal cellular yields. The lipid composition of cells cultivated five to six times was reduced by as much as fifty percent. Those cells cultivated more than six times had progressively greater quantities of lipid approaching that found in control cells. Those cells with reestablished lipid contents showed no further effects from more prolonged lead exposures. Chromatographic studies of each phase of cultivation revealed relatively complete lipid compositions. This indicates that where there were lipid reductions, lead had some inhibitory effect on a biochemical parameter in the biosynthesis of lipids (Peterson, et al., 1975).

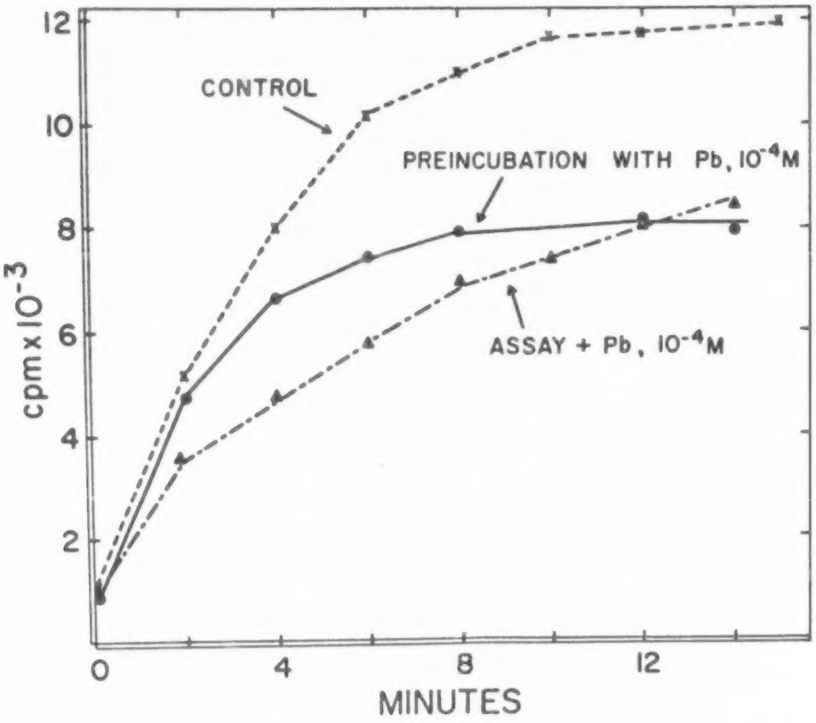

Figure 3.1 Effect of lead on incorporation of ^{14}C-leucine into t-RNA from E. coli. Addition of lead to the assay mixture decreases the rate of ^{14}C-leucine incorporation, most likely due to inhibition of the aminoacyl synthetase. Preincubation of t-RNA with lead at 37 C decreases the extent of amino acid incorporation, most likely due to hydrolysis of the nucleic acid. Source: Ulmer and Vallee. Reprinted with permission from Proceedings 2nd Annual Conference on Trace Substances in Environmental Health (c) University of Missouri, 1969.

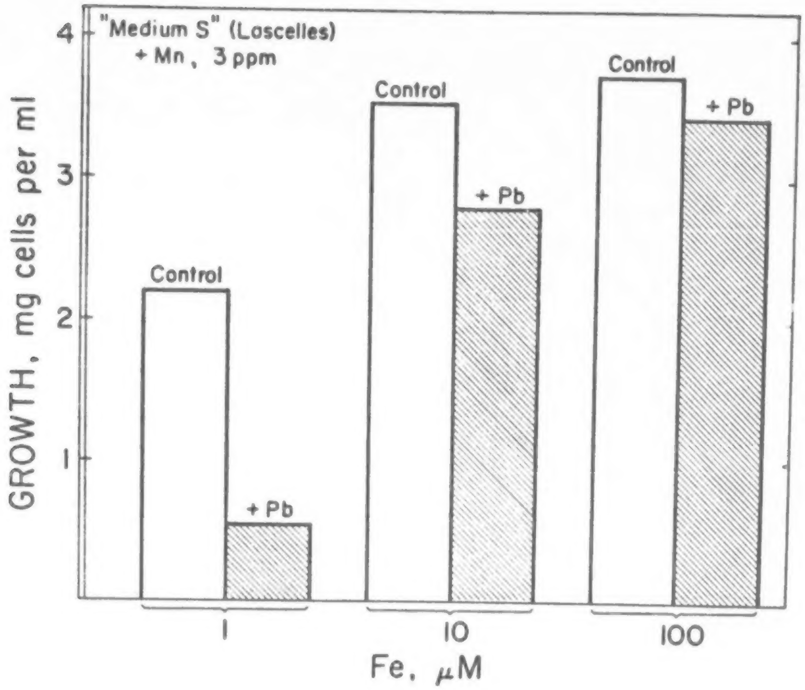

Figure 3.2 Effect of lead on growth of Rhodopseudomonas spheroides. At an iron concentration of 1 μM, lead markedly inhibits semianaerobic, light-grown cultures. This inhibition is largely overcome by higher iron concentrations.

Source: Ulmer and Vallee. Reprinted with permission from Proceedings 2nd Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1969.

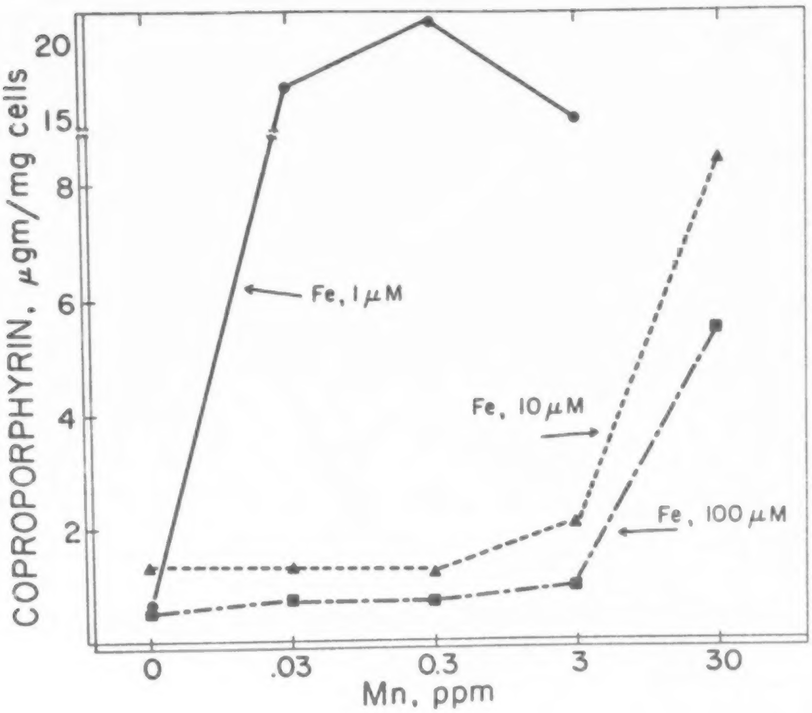

Figure 3.3 Metal-ion antagonism in Rhodopseudomonas spheroides. At low Fe concentrations (1 μM/liter) Mn, 0.03 ppm, induces marked coproporphyrin excretion. In the presence of 10 or 100 μM/liter Fe, increased coproporphyrin appears only at much greater Mn concentrations. Source: Ulmer and Vallee. Reprinted with permission from Proceedings 2nd Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1969.

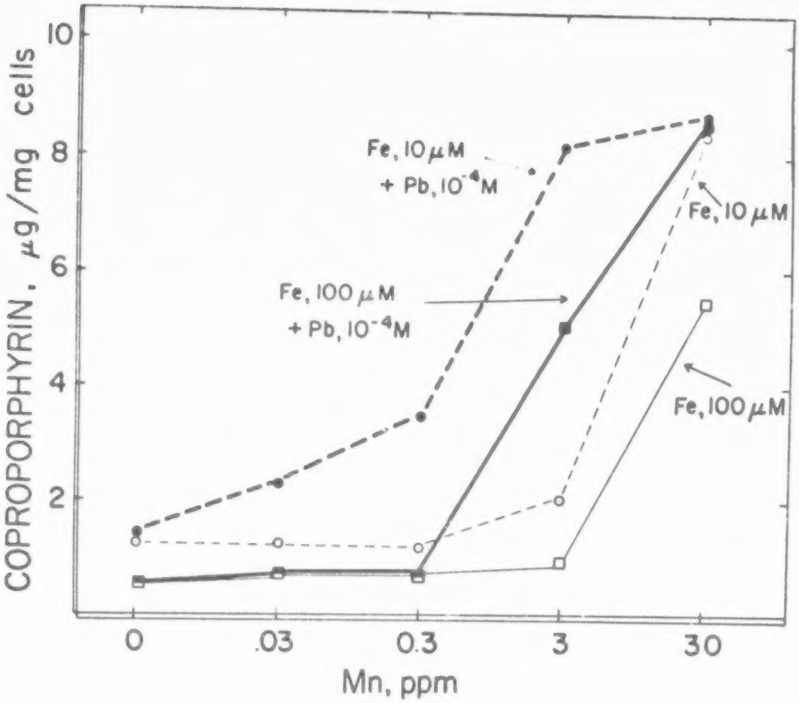

Figure 3.4 Synergistic antagonism of Fe by Mn and Pb in Rhodopseudomonas spheroides. In the presence of Pb, lesser concentrations of Mn induce coproporphyrin excretion. Source: Ulmer and Vallee. Reprinted with permission from Proceedings Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1969.

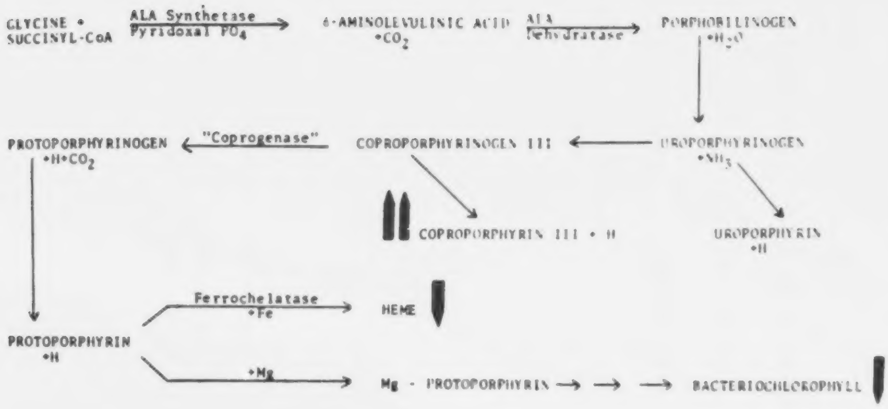
GLYCINE +
SUCCINYL-CoA
ALA Synthetase
Pyridoxal PO4
δ-AMINOLEVULINIC ACID
+CO2
ALA
Dehydratase
PORPHOBILINOGEN
+H2O
PROTOPORPHYRINOGEN
+H+CO2
"Coprogenase"
COPROPORPHYRINOGEN III
UROPORPHYRINOGEN
+NH3
COPROPORPHYRIN III + H
UROPORPHYRIN
+H
Ferrochelatase
+Fe
HEME
PROTOPORPHYRIN
+H
+Mg
Mg - PROTOPORPHYRIN
BACTERIOCHLOROPHYLL

Figure 3.5 Pathway of tetrapyrrole synthesis in Rhodopseudomonas spheroides. In the presence of Mn and Pb, coproporphyrin III is markedly increased while both principal end-products, heme and bacteriochlorophyll, are decreased (arrows). Source: Ulmer and Vallee. Reprinted with permission from Proceedings 2nd Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1969.

Table 3.2 EFFECT OF Pb AND Mn ON TETRAPYRROLE SYNTHESIS IN RHODOPSEUDOMONAS SPHEROIDES[a]

Metals Added[b]			A	B	C	D
Fe 1×10^{-6}M	Mn 2×10^{-5}M	Pb 1×10^{-4}M	Coproporphyrin, μg/mg[c]	Bacteriochlorophyll, μg/mg[c]	Heme, mμM/mg[c]	Protoporphyrin, μg/mg[c]
1	-	-	1.2	5.8	0.8	0.8
1	-	+	1.7	3.4	1.0	1.1
1	+	-	32.4	1.4	0.5	<1.0
1	+	+	36.8	1.4	0.5	<1.0
10	-	-	1.3	7.6	1.0	1.6
10	-	+	1.5	10.8	0.9	1.4
10	+	-	0.6	3.3	1.0	0.3
10	+	+	7.3	2.2	0.7	0.1

[a] Source: Ulmer and Vallee. Reprinted with permission from Proceedings 2nd Annual Conference on Trace Substances in Environmental Health. (C) University of Missouri, 1969.

[b] Lascelles Medium S with metals as indicated.

[c] Tetrapyrrole concentration per mg cell protein.

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4.0 EFFECTS ON PLANTS

4.1 SUMMARY

The presence of lead in plants has received considerable attention because of the potential hazard to animal and human health. Several sources including soil, water, and air give rise to lead in plants.

Ubiquitous concentrations of lead are found in most soils but their content varies according to the levels of lead in the parent material and to various physical factors such as the weathering rate. Higher lead levels in soil may be found near lead mines or industries using lead, where heavy-metal-containing sewage sludge has been spread, and adjacent to well-used roadways. Most of the lead compounds are deposited within a few meters of the road, with contamination being restricted to the topsoil.

Depending on the type of plant, there are generally two pathways available for lead to enter: uptake by the roots and uptake by the foliage. Lead is absorbed by plants from the soil, but generally not to any great extent. There are many factors that determine lead availability and association with plants, these include soil concentrations, pH, cation exchange capacity, presence of other nutrients, natural chelating agents, and the individuality of the plant species involved.

Lead in aerosol form can be absorbed by plant foliage and lead can accumulate in particulate form on the foliage from aerial fallout. Critical evidence on foliar absorption of lead is difficult to obtain because of an inability to experimentally differentiate between lead deposited on, and lead absorbed by, the foliar tissue. Deposition of lead on leaves is known to be controlled by characteristics of the aerosol (size, chemical composition, cloud density), the leaf surface (roughness, pubescence, moisture), and the environment in which the plant lives (relative humidity, wind speed). The extent of lead accumulation in plants from particulate aerosols is now thought to be minimal.

Lead concentrations within plant tissues are influenced by the factors listed above as well as by lead pollution intensity, proximity to roadways and lead industries, wind direction, distribution within plant organs, cellular localization, and the amount of lead removed by washing with water.

Lead inhibits growth, reduces photosynthesis, and interferes with cell division and regenerative processes in algae. Studies show considerable similarity of lead effect on _in vitro_ enzymes when care is taken to define the medium parameters. No algal species have been reported to have any built-up tolerance to lead. In contrast, lichens, some fungi, and bryophytes seem to have a pronounced, genetically-determined tolerance to lead. Some lead chelates and organolead compounds, however, are fungicidal. Lichens and bryophytes are capable of concentrating lead at levels that are much higher than environmental levels without any effects. In fact, mosses and Spanish moss (a vascular plant) are being used as bioindicators in regional and local atmospheric lead surveys.

Some of the effects of lead on vascular plants include: (1) inhibition of photosynthesis, transportation and water absorption; (2) reduction of chlorophyll and ATP synthesis; (3) inhibition of enzymes unique to the photosynthetic and respiratory processes; (4) reduction of mitosis and subsequent growth; and (5) acceleration of abscission or defoliation and pigmentation. Only one of the vascular plants, *Agrostis tenuis* (Rhode Island bent) seems to have the chemical ability to precipitate lead from cytoplasmic solution and thus render it inactive. The effects of lead on vascular plants appear at this stage to be minimal. Probably the most important adverse effects of lead from vascular plants are economic and may result from ingestion of topical plant lead by grazing animals.

Many metabolic processes can potentially be affected by lead since they are controlled or associated with enzymes having secondary or tertiary structures which are potentially capable of binding lead.

Environmentally, it would seem that a plant with sufficient nutrients, moisture, temperature and light would be unlikely to be affected by lead concentrations of less than 100 ppm in the plant tissue on a dry weight basis.

4.2 NONVASCULAR PLANTS

4.2.1 Algae

4.2.1.1 Metabolism: Uptake, Absorption, and Residues--

Very little is known of the background lead concentrations in algae. Most algal species probably have the capacity for concentration or uptake of lead to levels above that in the water medium. For example, the concentration factor (ratio of an element in an organism to the concentration available in the medium under equilibrium conditions) for lead by marine phytoplankton is 4×10^4 (National Academy of Sciences, 1971).

Day (1963) indicates that aquatic algae such as *Spirogyra* have the capacity to remove suprisingly large quantities of elements from their environment. *Spirogyra*, growing in mine water containing a total of 16 ppm heavy metals, contained 2,900 ppm zinc, 6,600 ppm lead, and 920 ppm copper (on a dry weight basis). Gale, et al., (1973) found 8,035 ppm lead associated with *Cladophora* taken 0.31 kilometer below a tailings dam in Missouri's New Lead Belt. There was a definite inverse linear relationship between lead concentration on or in the algae and distance from the source of contamination. Laboratory studies confirm that *Cladophora* happens to be one of the forms which has been found to attract and bind relatively large amounts of lead. The researchers indicate that the data are suggestive of rapid ion-exchange processes which bind the lead to the organic material of the algal cells.

4.2.1.2 Effects--

The usual procedure in assessment of toxic and other effects of heavy metals on algae is to observe the effect of the material on the test organism over a range of concentrations. For lead care must be taken to ensure solubility, since lead is easily precipitated from solution by sulfates, phosphates, chlorides, carbonates, etc. Even in demineralized water there are enough ions present to limit solubility of the lead ion.

Although there is a large amount of literature on the toxicity of lead to animals, and the literature is growing on toxicity to vascular plants, few studies have been conducted on the effects of lead on algae.

Most of the studies on effects have involved exposure to various concentrations of lead with observations of resultant effects. Rice, et al., (1973) reported that lead at 0.1 parts per million had no effect on the marine phytoplankton *Phaeodactylum tricornutum*, *Chaetoceros galvestonensis*, and *Cyclotella nana*, but did inhibit growth in the freshwater green alga *Chlorella*. Studies by Hannan and Patouillet (1972) are supportive: lead at 0.1 ppm and 1.0 ppm had no significant effect upon growth of *Phaeodactylum*, but lead at 0.1 ppm did inhibit temporarily growth by *Chlorella*. Banks (1972) exposed *Chlorella pyrenoidosa* to concentrations of 1.0 ppm and 10.0 ppm lead as lead acetate. Banks reported that 1.0 ppm of lead in modified Bristol's solution did not affect cell number or content of chlorophylls *a* and *b* during 15 days of culturing; however, 1.0 ppm lead in demineralized water decreased cell number by approximately 10 percent. At 10 ppm lead the number of cells was reduced to 52 percent of the control after 5 days. Although autospore formation was not impaired at this concentration, chlorophyll content was reduced after 15 days of culturing such that chlorophyll *a*, chlorophyll *b* and total chlorophyll were 46, 76, and 53 percent of the control, respectively. The presence of demineralized water does support the concept that the association of Pb^{++} with other ions in the growth medium and in the cells tends to complex lead and render it inactive metabolically.

Other investigations have reported that lead in solution inhibits algal growth. Monahan (1973) found that lead, as lead chloride, at concentrations which ranged from 50 through 500 ppm reduced cell density in cultures of the green alga *Hormotila blennista* under both light and dark environments. Whitton (1970) investigated a variety of natural algal populations to determine if any had built up a tolerance to heavy metal - zinc, copper, lead - pollution. No tolerance to elevated lead concentrations was found. The fixation of labelled CO_2 was used by Malanchuk and Gruendling (1973) to measure the toxicity of $Pb(NO_3)_2$ at 10, 20, and 30 ppm Pb to *Anabaena* sp., *Chlamydomonas reinhardti*, *Cosmarium botrytis*, *Navicula pelliculosa*, and *Ochromonas malhamensis*, all freshwater organisms. The concentration of lead which caused a 50 percent reduction of $^{14}CO_2$ fixation as compared to the control defined the ED_{50} (median effective dose). The ED_{50}'s reported by Malanchuk and Gruendling (1973) were 15 to 18 ppm Pb for *Anabaena*, *Chlamydomonas*, and *Navicula*; 5 ppm for *Cosmarium*; an ED_{50} for *Ochromonas* was not obtained. Lead nitrate at 4.1 ppm Pb produced no deleterious effects on the photosynthetic rate in giant kelp, *Macrocystis pyrifera*, during a 4-day exposure (North and Clendenning, 1958, cited in McKee and Wolf, 1963).

Light-induced oxygen evolution in *Chlamydomonas reinhardti* was inhibited by lead ions. This photosynthetic phase was found to be ten times as sensitive to cadmium and lead ions as it is to copper and mercury ions. In contrast, the chlorophycean *Dunaliella bioculata* exhibited decreasing sensitivity in the order: mercury, lead, cadmium (Overnell, 1975).

Hessler (1974 and 1975) has studied the effects of lethal and sublethal concentrations of lead chloride on the marine unicellular green flagellate alga, *Platymonas subcordiformis*. Lead concentrations between 2.5 and 10 ppm were sublethal to *P. subcordi formis* and delayed cell division and daughter cell separation. Lead at 60 ppm was lethal to the test organism. Hessler (1974) noted several abnormalities due to lead treatment of this alga: (1) loss and alteration of flagella, and (2) impairment of motility. In subsequent research, Hessler (1975) reported that the incidence of mutant types above spontaneous frequency in *P. subcordiformis* was not raised upon exposure of the alga to sublethal and lethal concentrations of lead.

Lead interferes with cap formation and regeneration in the unicellular marine alga, *Acetabularia mediterranea*. Bonotto and Kirchmann (1973) found that (1) cap formation, which is necessary for reproduction in *Acetabularia*, in nucleate as well as in anucleate cells is rapidly (4 days) inhibited by 1 to 10 ppm concentration of $Pb(NO_3)_2$, and (2) cap growth, regeneration of nucleate basal fragments, and growth of regenerating stalks are less sensitive to lead treatment than cap initiation which is the morphogenic process most sensitive to lead exposure.

Momentary bubbling of biologically-generated tetramethyllead (TML) into a culture of *Scenedesmus quadricauda* decreased primary productivity and cell growth by 85 and 32 percent, respectively, as compared to controls. Cells exposed to TML also tended to clump. Similar results were obtained with *Ankistrodesmus falcatus* (Wong, et al., 1975). Of the organometallic compounds used in algistatic tests, the triphenyllead and tributyllead adjuncts appeared to confer the greatest toxicity to *Enteromorpha* sp. Hexaphenyldilead also appeared to be an active algistat (Skinner, 1974).

4.2.2 Lichens, Fungi, and Bryophytes

4.2.2.1 Metabolism: Uptake, Absorption, and Residues--

Lichens have a marked capacity for inorganic cation uptake. In fact, some species, e.g., *Cladonia* spp. and *Stereocaulon* spp., appear as consistent components of mine communities. Puckett, et al., (1973) studied metal-ion uptake by lichens and found that iron, copper, and lead accumulations accounted for 76 to 87 percent of the total metal uptake. 4,144 to 4,310 ppm

Pb was absorbed by *Umbilicaria muhlenbergii* from lead nitrate solutions containing 16,575 ppm Pb *Cladonia mitis* and *U. muhlenbergii*, collected near a smelter, were found to contain 414 to 497, and 559 to 642 ppm Pb^{++}, respectively, as determined by total wet oxidation. Holl and Hampp (1975) cite the use of the lichen *Parmelia physodes* as a bioindicator for the intensity of lead emission. At a distance of 1,000 meters from the highway the thalli contained 35 ppm (unwashed) and 19 ppm (washed) lead.

Experimental studies of lead uptake in *Cladonia rangiformis* revealed that all the lead, whether taken up naturally or artificially, is bound in an exchangeable form to insoluble anionic sites within the cell wall. The association of lead was shown to take place in the presence of living cells and is therefore, considered to be a purely physical process. Samples of *C. rangiformis* collected in a relatively lead-free area versus a disused lead mining complex reflected the composition of the underlying soil. In the lead mining complex, lichens growing in soil containing 27,500 ppm lead had a lead concentration of 1,100 ppm. Those growing in the relatively lead-free area with a soil lead content of 20 ppm had a lead concentration of 25 ppm (Brown and Slingsby, 1972).

Only one reference to the uptake of lead by fungi has been found. Washed mycelia of *Aspergillus clavatus* cultured at 24 C in 1 percent glucose, 0.5 percent peptone, 0.5 percent yeast extract, and 1 gram per liter lead oxide concentrated 1,080 ppm lead after 35 days of exposure. The lead content of the culture medium was 32 ppm giving a resultant concentration ratio (mycelium:medium) of 34 (Siegel, et al., 1973).

Numerous species of mosses have been recorded as members of communities on metal-contaminated soils. Liverworts are much rarer on contaminated soils. Bryophytes (mosses and liverworts) growing in such areas or in relatively contamination-free areas have been found to have a greater lead content than the substrates on which they grow (see Table 4.1). Enrichment of upper soil horizons has been attributed to the action of these plants which concentrate elements and then, by decomposition, release them into the surface soil (Antonovics, et al., 1971; Shacklette, 1965a,b).

Mosses accumulate nutrients, including heavy metals, through their aerial regions. This association may arise from aerial particles or as ions from dilute solutions. These properties have allowed the use of certain mosses in monitoring short-term metal accumulation from aerosol and precipitation sources (Ratcliffe, 1975). Ruhling and Tyler (1970) showed that the woodland moss *Hylocomium splendens* absorbed heavy metal ions from dilute solutions in the order Cu > Pb > Ni > Cb > Zn > Mn. These observations were made over a wide range of concentrations and seem to be independent of other heavy metals or essential nutrients. *Rhytiediadelphus squarrosus* incorporated lead into the nuclei of cells of plants exposed to lead acetate solutions. Studies cited by Skaar, et al., (1973) revealed that ^{210}Pb was incorporated into both nuclear and mitochondrial fractions. Extracellular Pb binding has also been observed by Brown and Bates (1972) in *Grimmia doniana* by a passive physical process. Ratcliffe (1975) has presented evidence that a number of suspended moss samples including *Dicranella*

Table 4.1 LEAD CONTENT OF BRYOPHTYES AND THEIR SUBSTRATES[a]

Bryophyte Species	Ash, Percent[b]	Lead Content Ash Percent	Lead Content of Substrate, Percent[b]
Anomodon rostratus	9.5	0.03	0.0025 (soil)
A. rostratus	13.5	0.3	0.006 (limestone)
Atrichum angustatum	9.7	0.1	0.003 (soil)
Batramia pomiformis	26.5	0.015	0.002 (lithosol)
Bazzania trilobata	14.0	0.03	0.002 (soil)
Brachythecium rutabulum	11.8	0.05	0.003 (soil)
B. salebrosum	20.5	0.07	0.015 (soil)
Bryum capillare	10.0	0.03	0.005 (felsite porphyry)
Cirriphyllum boscii	11.7	0.05	0.001 (lithosol)
Climacium americanum	11.3	0.03	0.001 (lithosol)
Conocephalum conicum	13.0	0.05	<0.001 (limestone)
C. conicum	32.0	0.01	0.0075 (chert)
Dicranella heteromalla	7.0	0.07	<0.0025 (soil)
Dicranum scoparium	13.8	0.07	<0.001 (soil)
D. scoparium	12.0	2.0	0.01 (lithosol)
Entondon seductrix	13.5	0.07	0.015 (quartzose sandstone)
Grimmia apocarpa	11.3	0.2	0.01 (arkosic sandstone)
G. laevigata	41.0	0.03	0.0015 (granite)
Hedwigia ciliata	7.3	0.2	0.01 (arkosic sandstone)
H. ciliata	16.3	0.15	0.0025 (quartzose sandstone)
H. ciliata	5.7	0.15	0.0015 (granite)
H. ciliata	8.8	0.1	0.015 (quartzose sandstone)
H. cilita	10.3	0.3	0.006 (dolomite - limestone)
Hypnum curvifolium	8.7	0.07	0.001 (lithosol)
Leucobryum glaucum	1.67	2.0	0.01 (lithosol)
Marchantia polymorpha	59.5	0.0025	0.0015 (soil)

TABLE 4.1 LEAD CONTENT OF BRYOPHYTES AND THEIR SUBSTRATES[a]
(Continued)

Bryophyte Species	Ash, Percent[b]	Lead Content Ash Percent	Lead Content of Substrate, Percent[b]
Mnium affine	46.8	0.002	0.0015 (soil)
M. cuspidatum	8.3	0.07	0.0015 (soil)
Polytrichum commune	8.0	0.1	0.0015 (rock asphalt)
P. juniperinum	3.5	0.02	0.001 (soil)'
P. juniperinum	8.2	0.07	0.003 (soil)
P. juniperinum	8.3	0.07	0.0025 (soil)
P. ohioense	8.7	0.1	0.0015 (granite)
Thelia asprella	13.3	0.03	0.015 (bark of *Juniperus virginiana*)
T. lescurii	12.7	0.03	0.003 (lithosol)
Thuidium recognitum	10.2	0.05	0.001 (lithosol)
Weisia microstoma	15.2	0.3	0.006 (dolomite limestone)
W. viridula	17.3	0.05	<0.001 (dolomite limestone)

[a] Adapted from Shacklette (1965b).

[b] Dry weight basis.

heteromalla, Ceratodon purpureus, Sphagnum papillosum, and S. subsecundum can be used to monitor atmospheric lead fallout from a battery factory.

As with other mosses, Hypnum cupressiforme var. filiforme rapidly comes to equilibrium with aerial lead and other heavy metal concentrations. This species loses lead very slowly (Roberts and Goodman, 1973). Briggs (1972) found that lead values in Marchantia polymorpha, even at great distances from roads, were due to contamination. The lead contents corresponded to the respective traffic intensity and did not significantly correlate with the soil lead content.

4.2.2.2 Effects--

Lead was determined by Brown and Slingsby (1972) to be almost exclusively ionically-bound within the cell walls of lichens. These authors believe that under natural conditions, although excessive quantities of this potentially toxic element have been recorded from the thalli of lichens, lead is unlikely to have any direct effects on metabolism of the lichen. No other reference to toxicity of lead to lichens has been found in the sources searched.

Free lead ions at 269 ppm slightly reduced the accumulation of but did not suppress spore formation in the fungus Aspergillus niger. Because of their poor solubility in water, inorganic lead salts in a culture medium are not toxic to A. niger. Chelates such as lead thiopicolinanilide or lead diethyldithiocarbamate have strong fungicidal properties (Zlochevskaya and Rabotnova, 1966; Zlochevskaya and Rukhadze, 1968). Twenty-three organolead compounds were screened for fungicidal activity against sixteen fungal species isolated from paint films. Three of the compounds (tributyllead 2-ethyl hexanoate, tributyllead acetate, and triphenyllead acetate) exhibited fungicidal activity at 0.01 percent lead in unweathered and leached vinyl copolymer emulsion paint systems. Tributyllead acetate (0.05 percent lead) was fungicidal in a vinyl copolymer paint even after 250 hours of artificial weathering (Skinner, 1974).

Although fungi have been shown to be consistent, if not abundant, components of mine soils, there is surprisingly little evidence of tolerant races among the fungi. A tolerant species of penicillium which withstands external lead concentrations of 100 times those of nontolerant species has been found to be associated with a nonnuclear plasmid.

4.3 VASCULAR PLANTS

4.3.1 Noncrop Plants

4.3.1.1 Metabolism: Uptake, Absorption, and Residues--

The amount of lead reported in plant material varies widely and is dependent on lead levels in the plant's environment. Natural or background lead concentrations in the ash of several native plant species sampled from a variety of geochemical environments have been summarized by Connor and Shacklette (1975) and are included in Table 4.2.

Lead taken up by aquatic vegetation is believed to be bound primarily to the surface. Available evidence suggests that lead is bound to anionic sites on the surface of aquatic plants by the process of cation exchange. Gale, et al., (1975) found that extensive washing of aquatic vegetation from the New Lead Belt of Missouri in distilled, tap, or stream water failed to remove the bound lead. *Scirpus americanus* has a capacity for concentrating lead from its environment such that it is thought to be capable of serving as a depolluting agent. *Eleocharis smallii* and *Bidens cernua* are possibly capable of doing the same. *Scirpus*, *Eleocharis*, and *Bidens* were exposed to solutions containing 0.5 to 1.5 ppm lead for 72 hours. In the 1.5-ppm lead environment, the stems and rhizomes of *S. americanus* accumulated 54 and 885 ppm, respectively. In the same environment *E. smallii* accumulated 342 ppm in stems and 3,320 ppm in rhizomes. *B. cernua* accumulated 140 and 625 ppm in stems and rhizomes, respectively; the flowers and leaves had 28.3 ppm (Carbonneau and Tremblay, 1972). Analyses of shoots of *Spartina alterniflora* (cordgrass) growing in several salt marshes in Massachusetts revealed that they contained 5.4 to 23.2 ppm Pb on a dry weight basis. Increased contamination, either from the proximity to human activity or through the experimental additions of fertilizer, resulted in greater lead concentrations in the plants (Banus, et al., 1974). Drifmeyer and Odum (1975) studied the effect of the disposal of heavy-metal-containing dredge-spoil as a source of heavy metals to salt-marsh biota. The authors found that lead levels in *Phragmites communis* (common reed), *Spartina alterniflora* (salt-marsh cordgrass), and *S. patens* (saltmeadow hay) were significantly higher in plants growing on the dredge-spoil sites than in the control areas. Lead accumulation values were as follows for the three plant species: *P. communis*, 4.4 plus or minus 5.3 ppm (dredge-spoil) and 0.5 plus or minus 0.6 ppm (natural marsh); *S. alterniflora*, 5.1 plus or minus 1.2 ppm (dredge spoil) and 1.9 plus or minus 0.7 ppm (natural marsh); and *S. patens*, 9.1 plus or minus 2.9 ppm (dredge-spoil) and 0.8 plus or minus 1.4 ppm (natural marsh).

Spanish moss (*Tillandsia usneoides*) has been used as an indicator of atmospheric lead pollution since it is an epiphyte which derives all its nutrients from the air by means of leaf and stem absorption. Martinez, et al., (1971) analyzed eight Spanish moss samples from sites near and at some distance (0.16 to 0.48 kilometer) from heavily-traveled roadways. They found lead concentrations were greatest in samples taken near highways, with a maximum of 0.085 percent (850 ppm) in dry samples, whereas those more distant from highways contained as little as 0.0051 percent (51 ppm). Shacklette and Connor (1973) confirmed the above findings and noted that the typical lead concentration is the ash of 123 Spanish moss samples (70 to 50,000 ppm) exceeded the upper limit of the expected 67 percent range (8,800 to 45,000 ppm) in comparison to the lead content of the ash of soil-rooted plants (1,600 to 400,000 ppm) from the conterminous United States. Greater-than-average amounts of lead were found in samples from industrial and highway locations. The extremely high lead concentrations reflect the fact that most samples were taken at sites near highways.

Table 4.2 NATURAL LEAD LEVELS IN THE ASH OF NATIVE, NON-CROP U.S. PLANTS[a]

Sample and Collection Locality	Observed Range, ppm	Mean, ppm	Geometric Deviation
Black cherry, stems; Georgia	30 - 1,000	210	2.71
	<10 - 2,000	270	4.64
Black cherry, leaves; Georgia	<10 - 700	33	4.65
	<10 - 500	58	2.40
Blackgum, stems; Georgia	<10 - 1,000	250	2.88
	70 - 3,000	480	2.34
Blackgum, leaves: Georgia	<10 - 2,000	57	2.01
	10 - 1,000	96	2.56
Buckbush; Missouri			
Glaciated prairie	50 - 500	200	1.76
Unglaciated prairie	70 - 1,000	210	1.91
Cedar glade	100 - 2,000	300	1.85
Oak-hickory forest	70 - 1,000	260	1.88
Oak-hickory-pine forest	150 - 1,500	420	1.84
Cedar; Missouri			
Cedar glade	30 - 1,500	100	2.06
Glaciated prairie	50 - 200	86	1.54
Unglaciated prairie	70 - 150	91	1.42
Cedar glade	50 - 100	70	1.26
Oak-hickory forest	50 - 1,500	120	3.25
Oak-hickory-pine forest	20 - 200	64	2.16
Hickory, pignut; Kentucky	100 - 700	210	1.61
	120 - 940	260	1.51
Hickory, shagbark; Kentucky	70 - 500	170	1.57
	80 - 510	220	1.65
Hickory, shagbard; Missouri			
Oak-hickory forest	30 - 200	100	1.66
Oak-hickory-pine forest	100 - 300	190	1.65
Maple, red, stems; Georgia	<10 - 700	120	2.59
	30 - 2,000	230	3.13
Maple, red, leaves; Georgia	<10 - 700	41	2.92
	30 - 700	100	2.21

Table 4.2 NATURAL LEAD LEVELS IN THE ASH OF NATIVE, NON-CROP U.S. PLANTS[a]
(Continued)

Sample and Collection Locality	Observed Range, ppm	Mean, ppm	Geometric Deviation
Oak, black; Kentucky	70 - 500	150	1.63
	63 - 240	140	1.46
Oak, post; cedar glade; Missouri	30 - 700	80	1.87
Oak, red; Kentucky	70 - 200	120	1.34
	90 - 260	150	1.52
Oak, white; Kentucky	10 - 700	150	1.92
	50 - 440	180	1.49
Oak, white; Missouri			
Oak-hickory forest	30 - 500	100	1.85
Oak-hickory-pine forest	50 - 1,000	140	1.72
Oak, willow; floodplain forest; Missouri	30 - 500	120	1.85
Persimmon, stems; Georgia	<10 - 700	110	2.90
	<10 - 1,500	150	3.85
Persimmon, leaves; Georgia	<10 - 700	24	4.13
	<10 - 500	68	2.59
Pine, shortleaf; oak-hickory-pine forest; Missouri	100 - 1,500	250	1.70
Sassafras, stems; Georgia	30 - 700	210	2.37
	<10 - 1,000	140	4.91
Sassafras, leaves; Georgia	30 - 200	83	1.66
	30 - 500	95	2.28
Sumac, winged, stems; Georgia	<10 - 1,500	110	3.91
	<10 - 700	110	3.09
Sumac, winged, leaves; Georgia	<10 - 500	67	2.29
	30 - 700	120	2.25
Sumac, smooth; Missouri			
Floodplain forest	<20 - 200	26	2.28
Glaciated prairie	<20 - 100	32	1.82
Unglaciated prairie	<20 - 150	28	2.11
Cedar glade	<20 - 150	42	2.17
Oak-hickory forest	<20 - 150	30	2.36
Oak-hickory-pine forest	<20 - 300	61	2.23
Sweetgum, stems; Georgia	<10 - 700	120	2.86
	<10 - 700	110	3.31
Sweetgum, leaves; Georgia	<10 - 200	45	2.47
	20 - 300	91	2.07
Sweetgum; floodplain forest; Missouri	20 - 300	65	2.09

[a] Adapted from Connor and Shacklette (1975).

Sewage sludge from an urban-industrialized area of Atlanta, Georgia, containing high levels (up to 2,750 ppm) of lead were sodded to fescue (Festuca arundinacea). 1754 ppm increased the lead content of the plant tissue from 3 to 120 times. Additions of microelements to the sewage sludge doubled the amount of lead in fescue tissue above that contained with sewage sludge treatments alone (Boswell, 1975).

Wild oats (Avena fatua L.) have been proved to be a sensitive indicator of atmospheric inputs of lead (Rains, 1975). Dried plant material sampled for two seasons accumulated lead from the atmosphere with little or no inputs from lead-contaminated soils. The contaminated, above-ground plant tissue was also shown to retain lead deposited thereon from the atmosphere during the growing season, with only small amounts contributed from the soil. The wild oats were very sensitive to changes in input levels of atmospheric lead. A nearby smelter was closed during the winter after the first growing season. In the following year, the lead content was only a fraction of the content in the previous growing season. Similar results were obtained by Rains (1971). Leaching with water and the winter rains were ineffective in removing lead from the tissue.

Jones, et al., (1973a) found that the uptake of lead by intact perennial ryegrass (Lolium perenne var. 523) plants in solution cultures containing lead nitrate was very rapid and complete. Lead bound in roots was not released by exchange with calcium or barium ions. The total uptake, or lead burden, increased with increasing rates of lead addition and ranged from 280 to 9,970 micrograms of lead per three plants harvested. The concentration of lead in shoots at the first harvest ranged from 0.2 to 58.4 ppm and that in the corresponding roots from 5.5 to 5,310 ppm. Jones, et al., (1973b) studied the lead status of sixteen soils in which perennial ryegrass was grown, with and without added sulfur, in a controlled environment cabinet with carbon-filtered air. The lead concentration in the tops of healthy plants (those with adequate sulfur) was lower than in the roots. The mean lead content at the fourth harvest was 5.0 and 12.9 ppm, respectively, in the tops and roots. Marked increases in lead concentration in the tops of sulfur-deficient plants coincided with decreases in dry-matter yield.

Ter Haar, et al., (1969) utilized specially-constructed chambers in a greenhouse for experiments to determine uptake and retention of lead by perennial ryegrass and radishes. Ryegrass plants were grown in normal (0.96 microgram Pb per cubic meter) or filtered air (0.03 microgram Pb per cubic meter) while distilled water or water containing 40 micrograms Pb as $PbCl_2$ per liter was applied either to the leaves or soil surface. The lead content of grass grown in filtered air was 2.5 ppm while that grown in unfiltered air was 5.2 ppm. The mean lead concentration in grass grown with distilled water was 4 ppm; with lead-containing water, 3.9 ppm; under foliar application of water, 4 ppm; and under soil application, 3.7 ppm. These data compare favorably with the respective values of 4.9 ppm and 3.5 ppm reported by Jones and Hatch (1945) and Marten and Hammond (1966). Dedolph, et al., (1970), in experiments designed to determine the contribution of lead in soil, water, and air to that in perennial ryegrass and radishes, found that ryegrass derived 2 to 3 ppm Pb from soil sources. Leaf-lead levels in excess of that from soil were derived from, and quantitatively related to atmospheric concentrations in the growth chambers (an average of 0.09 and 1.45 micrograms Pb per cubic meter, respectively, in filtered and unfiltered air). Lead added to water at 40 micrograms per liter as $PbCl_2$ did not affect the concentration in the grass.

Marten and Hammond (1966) grew bromegrass plants which had been propagated from the same clone in lead-contaminated soils. Three crops were harvested; after the second harvest chelates were added to the soils. The most significant fact derived from the experiment was that even the greatest grass lead concentration (34.5 ppm) was far below that which would be toxic to animals consuming the grass. The addition of the chelates resulted in a distinct rise in lead concentration only in grass growing in the most contaminated soils.

The removal of metals by 30-day-old barley seedlings (Hordeum vulgare L., cv. Traill) from two topographically associated soils having pH's of 5.9 and 7.9 (free carbonates) was studied following the application of 0.35, 6.9, 13.8 and 27.6 metric tons (0, 3.8, 7.6, 15.2, and 30.4 tons) per hectare of sewage sludge (Dowdy and Larson, 1975a). The total uptake of zinc, lead, nickel, and chromium was greater from the sludge-amended acid soil than from the calcareous soil. Lead uptake increased by 50 percent with the addition of 27.3 metric tons (30 tons) per hectare.

Rolfe (1973) studied lead uptake by seedlings of eight tree species. Experiments were done with additive lead chloride additions from 0 to 600 parts per million, and additive phosphate additions from 0 to 336 kilograms per hectare. The uptake of lead was reduced to approximately 1/2 when the higher level of phosphate was added to the soil.

An area of immense concern is that of lead uptake by vegetation near well-traveled roadways or lead-producing or lead-utilizing industries (mines, mills, and smelters). Dedolph, et al., (1970) obtained average lead concentrations of 15, 8.4, and 7.9 ppm dry weight, respectively, in leaves of ryegrass grown in field plots 12.2, 36.6, and 155 meters (40, 120, and 510 feet) from the road. Hemphill (1974) and Hemphill, et al., (1974) found that forage plants and soils along ore-truck routes in Missouri's Lead Belt contained elevated levels of lead and other toxic metals, which decreased with increasing distance from the highway. Lead concentrations in or on unwashed vegetation along the ore-truck routes averaged 280 ppm dry weights on the road right-of-way, and 34 ppm at 91.4 meters (100 yards), 11.6 ppm at 182 meters (200 yards), and 6.5 ppm at 365 meters (400 yards) from the highway. Blueberries had a maximum of 537 ppm along the truck routes and 172 ppm at 91.4 meters from the routes.

Evidence for the accumulation of toxic levels of lead in forage plants was the deaths of several horses beginning in 1970 (see Section 5.5.2). Lagerwerff and Specht (1970) found that lead concentrations in grass samples (tall fescue, bluegrass, and orchard grass) decreased with distance from traffic. The concentration also decreased with depth in soil profiles. According to a study conducted by Graham and Kalman (1974), lead levels in grass at all points up to 91 meters from the roadway in a suburban setting surpassed the amounts that are potentially hazardous to horses and cattle. In fact, the levels were nearly 200 times that of natural levels of 5 ppm as reported by Motto, et al., (1970). A limited number of observations by Graham and Kalman (1974) also indicated an inverse relationship between concentration of lead and distance from roads as has been verified by Schuck and Locke (1970) and Page, et al., (1971). Tables 4.3 and 4.4 further summarize somewhat different findings of lead in grasses as related to distance from traffic or industry.

On- and off-road samples of plants from Missouri were analyzed for the presence of lead. All vegetation clearly showed a roadside effect. Grass samples from Kansas City averaged 29 and 9.7 ppm of lead, respectively, in on- and off-road samples; those from Pacific averaged 17 ppm and 4.5 ppm. Red cedar trees (Juniperus virginiana), sampled at widely scattered sites in southern Missouri, averaged 16 ppm in on-road samples and 7 ppm in off-road samples. One cedar tree sampled in Centerville, a major lead-mining district, had 1,200 ppm lead. Cedars and grass growing within 15.2 meters (50 feet) of pavement had lead contents two to three times the amounts found in companion species taken 91.4 meters (300 feet) from the pavement (Connor, et al., 1971a). An intensive study of cedars in Centerville, Missouri, showed a geometric mean concentration of 5,800 ppm lead in the ash of fifteen samples. Such high concentrations were considered to be a roadside effect and to reflect vehicular transport of lead-bearing ores from mine to smelter, rather than an unusual occurrence of lead minerals in the bedrock (Conner, et al., 1971b).

Keith (1969) analyzed elm, maple, and oak trees and soils from the Upper Mississippi Valley mining district, and from an area outside but continguous to the district for lead and zinc content. Stems contained about twice as much lead (78 to 135 ppm from the mineralized area; 102 to 150 ppm, nonmineralized area) as did the leaves (26 to 62 ppm, mineralized area; 29 to 61 ppm, nonmineralized area) from the same stems. Lead appeared to be slightly more concentrated in trees from the nonmineralized area whereas zinc was more highly concentrated in trees from the mineralized area. This can possibly be explained as a function of regional geology. Outside the mining district, more acidic conditions prevailed. These conditions allowed for the solubility and mobility of lead compounds. Buchauer (1973) found that a statistically significant correlation existed among lead contents for six tree species growing near two zinc smelters. Red oak seedlings were planted at various distances from one of the smelters. The surviving seedlings were harvested and analyzed after two growing seasons. At distances of 1 to 40 kilometers from the smelter, leaves had 100 to 11 ppm; stems, 35 to less than 10 ppm; and taproots, less than 100 ppm of lead, respectively.

Hemphill and Pierce (1975) studied the accumulation of lead in or on vegetation in an area in Missouri's New Lead Belt which encompassed four mines and mills and one smelter, and an area outside the New Lead Belt with a smelter at the center. The data summarized in Tables 4.5 and 4.6 show that vegetation in the near vicinity of smelters and, to a lesser extent,

Table 4.3 LEAD IN GRASSES AS A FUNCTION OF DISTANCE FROM TRAFFIC OR INDUSTRIES

Distance from Road, m	Lead Content, ppm, dry weight	References
0 - 7.5	80[a]	Cannon and Bowles (1962)
7.5 - 15	66	
15 - 150	45	
Over 150	20	
0	664[b]	Motto et al., (1970)
7.5	454	
23	198	
37.5	139	
67.5	68	
Region of a smelter	500[c]	Rains (1971)
7.6 - 30	20 - 60	Chow (1970)
0 - 336.7	8 - 341 (fescue)	Hemphill et al., (1974)
0 - 336.7	5.8 - 344 (purple top)	
8 - 32 (U.S. 1, Beltsville, Maryland)	26.3 - 68.2	Lagerwerff and Specht (1970)
8 - 32 (Washington-Baltimore Parkway, Bladensburg, Maryland)	18.5 - 51.3	
8 - 32 (I-29, Platte City, Missouri)	7.5 - 21.3	
8 - 32 (Seymour Road, Cincinnati, Ohio)	7.6 - 31.3	

[a] Ash; average content.
[b] Highest values from unwashed grass samples.
[c] Highest value from a survey of four seasons.

Table 4.4 LEAD IN ROADSIDE GRASS SAMPLES[a]

Distance from Highway, ft	12,800 Vehicles per 24 hr	14,700 Vehicles per 24 hr	17,700 Vehicles per 24 hr	19,700 Vehicles per 24 hr	41,000 Vehicles per 24 hr	45,600 Vehicles per 24 hr	48,600 Vehicles per 24 hr	48,600 Vehicles per 24 hr	54,700 Vehicles per 24 hr	Average
Lead Content, Not Washed, ppm										
0	–	–	–	133	141	118	–	664	219	255.0
25	63	–	–	84	66	192	154	454	139	164.6
75	76	–	–	65	103	–	66	198	83	98.5
125	–	–	31	41	–	66	45	139	78	66.7
175	–	–	–	41	60	46	66	–	61	54.8
225	–	35	–	34	56	41	48	68	59	46.3
Av.	–	–	–	66.3	85.2	92.6	75.8	304.6	106.5	112.0
Lead Content, Washed, ppm										
0	40	40	91	133	136	71	128	492	98	136.6
25	37	23	64	58	85	80	62	262	83	83.8
75	64	34	46	59	80	–	50	77	60	58.8
125	58	43	26	58	55	46	36	59	45	47.3
175	47	35	–	18	46	31	45	–	62	40.6
225	50	31	–	36	58	32	31	44	43	40.6
Av.	49.3	34.3	56.8	60.3	76.7	52.0	58.7	186.8	65.2	69.8

[a] Source: Motto, et al., Reprinted with permission from Environmental Science and Technology. (c) American Chemical Society, 1970.

Table 4.5 CONCENTRATION OF LEAD IN LEAVES OF POST OAK (*Quercus stellata*) AND NEEDLES OF SHORTLEAF PINE (*Pinus echinata*) IN VICINITY OF LEAD SMELTER OPERATIONS[a]

	Micrograms per Gram - Dry Weight			
	Post Oak		Shortleaf Pine	
Distance from Smelter (mi.)	Range of Values	Mean	Range of Values	Mean
0 - 0.5	230-8125	3776.70	420-11750	3546.36
0.5 - 1.0	71-3800	771.40	101- 1475	497.37
1.0 - 1.5	50-1580	250.00	52- 1050	273.56
1.5 - 2.0	45- 640	192.80	62- 412	142.85
More than 2.0	18-1360	168.97	22- 661	123.29

[a] Adapted from Hemphill and Pierce (1975).

Table 4.6 CONCENTRATION OF LEAD IN LEAVES OF WHITE OAK (*Quercus alba*) AND LEAVES OF BLUEBERRY (*Vaccinium pallidum*) IN VICINITY OF LEAD PROCESSING OPERATIONS

	Micrograms per gram - Dry Weight					
	White Oak			Blueberry		
Distance Miles	Range of Values	Mean	n	Range of Values	Mean	n
			Fletcher Mine and Mill			
0 - 1	39.0	39.0	1	39.0 -132.0	85.5	2
1 - 2	16.5 - 70.0	35.9	6	16.5 - 40.0	25.8	5
2 - 3	20.0 - 26.5	22.6	6	16.5 - 27.5	20.6	5
3 - 4	10.8 - 57.7	20.7	10	11.5 - 42.5	20.6	12
4 - 5	12.5 -124.0	29.5	15	5.8 - 73.9	27.1	17
5 - 6	12.5 - 36.5	22.6	11	5.9 - 24.0	17.7	11
			In Vicinity of Smelter			
1 - 2	75.8 -1221.0	574.3	3	141.0 -874.0	495.3	3
2 - 3	122.0 - 557.0	299.0	7	93.0 -338.0	203.9	10
3 - 4	39.8 - 155.0	80.2	4	21.0 -146.0	76.1	5
4 - 5	28.2 - 276.0	93.0	10	34.2 -181.0	68.6	11
5 - 6	23.5 - 228.0	75.6	12	24.0 -155.0	64.3	10
6 - 7	26.0 - 121.0	54.5	9	29.0 -101.0	41.6	11

[a] Adapted from Hemphill and Pierce (1975).

in the vicinity of mines and mills, accumulated levels of lead that are manyfold that of background levels.

Six species of trees (sugar maple, pin oak, yew, Norway maple, Eastern hemlock, and Norway spruce) growing in the City of New Haven, Connecticut, were found to have a mean lead tissue concentration in the preceding growing season that exceeded most lead concentrations determined for trees in areas with geologic lead deposits or adjacent to primary highways (Smith, 1972; Smith, 1973). Washing and analysis with an electron microprobe failed to provide conclusive evidence with regard to the specific location of the lead on or in the tissue sampled. The highest lead concentrations were associated with the leaves of pin oak and Norway maple. The maximum lead concentration observed was 760 ppm dry weight in a washed hemlock twig (see Table 4.7). In contrast, Smith (1973) found that twigs and leaves of sugar maple growing in remote sections of northern New Hampshire and Vermont contained 0 to 20 ppm lead on a dry weight basis. The analysis of bark from white pine (*Pinus strobus*) and elm (*Ulmus americanus*) trees growing adjacent to densely travelled streets with an electron probe microanalyzer revealed that lead, chlorine, and bromine were associated with particles, about 7 micrometers in diameter, held on the rough surface or embedded in the surface cells of the bark (Heichel and Hankin, 1972). Heretofore, there has been no information on the form or composition of lead residues on or in plants. These findings show that lead on or embedded in plant surfaces, especially rough ones, may be associated with at least two other elements, chlorine and bromine, and suggests their origin from automobile exhausts. Using an aerosol generator and wind tunnel fumigation system, Wedding, et al., (1975) found that the gross deposition of lead aerosols on rough, pubescent leaves of sunflowers (Helianthus annuus L.) was ten times greater than on the smooth, waxy leaves of the tulip poplar (Liriodendron tulipifera). The findings of Page, et al., (1971) with consumer crops confirm the above data on lead aerosol deposition on plant leaves (see Section 4.3.2.1).

4.3.1.2 *Effects*--

There is surprisingly little information in the open literature on the effects of lead and its compounds on vascular, noncrop plants. However, it is reasonable to expect similar effects (reduction of photosynthesis, mitosis, and water absorption) on many species of this group of plants as have been shown for vascular, crop plants (see Section 4.3.2.2).

Low lead concentrations (as lead acetate) reduced root growth and leaf and flower production of hyacinth bulbs (Holl and Hampp, 1975; National Academy of Sciences, 1972). *Bougainvillaea* sp. (five plants) exposed to approximately 7 ppm tetraethyllead vapor at 25 C for a 3-day period exhibited 14 percent defoliation or abscission. Fourteen days were required for total recovery from the 3-day, organolead exposure (Siegel, et al., 1973).

Root growth of sheep fescue (*Festuca ovina*) was retarded, markedly reduced, and stopped by 10, 30, and 100 ppm of $Pb(NO_3)_2$, respectively. Three parts per million lead in the form of a pure lead nitrate solution was highly toxic to all plants of *F. ovina*, while in a Knopp's culture medium

Table 4.7 LEAD BURDENS OF TREES GROWING IN THE CITY OF NEW HAVEN, CONNECTICUT[a]

Species	Tissue Analyzed		Lead (micrograms per gram, dry weight)	
	Organ	Number of Trees	Unwashed	Washed
Pin oak (*Quercus palustris*)	Leaves	12	70-200	55-220
	Twigs	12	25-110	25-125
Sugar maple (*Acer saccharum*)	Leaves	7	25-315	35-120
	Twigs	7	21-315	38-195
Norway maple (*Acer platanoides*)	Leaves	32	20-515	45-485
	Twigs	32	25-290	10-300
Eastern hemlock (*Tsuga canadensis*)	Leaves	8	40-203	25-180
	Twigs	8	97-510	155-760
Yew (*Taxus* spp.)	Leaves	10	50-318	70-371
	Twigs	10	50-318	70-371
Norway spruce (*Picea abies*)	Leaves	4	100-390	100-240
	Twigs	4	100-390	100-240

[a] Source: Smith. Reprinted with permission from Environmental Science and Technology. (c) American Chemical Society, 1973.

many plants showed little reduction in root growth at 25 ppm. Certain nutrients in the medium obviously had an antagonistic effect on the toxicity of lead (Wilkins, 1957). Tests have shown that plants (Agrostis tenuis, Deschampsia flexuosa, Festuca ovina) grown near a lead mine exhibited a low sensitivity to lead. In addition, calcium was found to ameliorate lead toxicity in F. ovina and A. tenuis. Lead-resistant A. tenuis populations exhibit an adaptation to very low calcium and phosphate concentrations. High lead contents of soil lower phosphate concentrations which are essential for plants. The need of plants for calcium diminishes in the absence of large concentrations of heavy metals. Generally, plants show a greater susceptibility to heavy metals when their calcium content is small. Lead tolerance in F. ovina is genetic involving a single gene (Antonovics, et al., 1971; Bradshaw, 1952; Holl and Hampp, 1975; Lagerwerff, et al., 1973; NAS, 1972; Wilkins, 1957).

Perennial ryegrass (Lolium perenne var. S23) roots showed a pronounced blackening at the tips similar to that described by other investigators for onions, beans, and maize after exposure to lead nitrate in solution (Jones, et al., 1973a). Relatively low concentrations of lead inhibited photosynthesis and transpiration of detached sunflower leaves (Hilianthus annuus) primarily by interfering with stomatal function. The degree of stomatal opening was determined experimentally to decrease log-linearly with increasing concentrations of lead from 10 to 1,000 micromoles. Net photosynthesis was reduced by 50 percent when leaf tissue lead concentrations were 0.93 micromole per gram (193 ppm). Transpiration was similarly reduced (Bazzaz, et al., 1974a).

Whole plant studies of the effect of lead, cadmium, nickel, and thallium on net photosynthesis and transpiration were conducted by Carlson, et al., (1975) to obtain some measure of the damage of heavy metals to physiological processes taking place in the leaves of intact plants. Corn and sunflower plants were grown in hydroponic culture and treated with various levels of lead chloride and other metal salts. Lead did not cause a statistically significant reduction in net photosynthesis at the treatment levels used. Even at lead concentrations up to 500 ppm, net photosynthetic and transpiration rates of lead-treated plants were not significantly different than those of control plants. These data suggest that lead is not translocated in appreciable quantities from hydroponic media through the root system and into leaf tissue of intact plants during short-term experiments.

Lead chloride concentrations of 41 to 410 ppm in watering solutions reduced the height, stem and root dry weights, and root/shoot ratio of loblolly pine (Pinus taeda) and red maple (Acer rubrum) seedlings in two forest soils. Increasing amounts of lead resulted in progressively smaller pine needles accompanied by the appearance of a milky-green hue, and, finally, in overall necrosis at the higher levels. The root systems also became reduced and blackened. Lead treatments caused an increase in red pigmentation (anthocyanin content) and an accelerated casting of red maple leaves (Davis and Barnes, 1973).

Little (1973), in a study of heavy metal contamination of tree leaves (Ulmus glabra, elm; Crataegus monogyna, hawthorn; Salix alba, willow;

Quercus robur, oak), concluded that considerable proportions of the total lead burden are removed by washing. Since much of the metal appears to be bound to membranes and cell walls and only small amounts are released on boiling, it seems likely that comparatively small amounts of the metal are metabolically active within the leaves. This might offer an explanation for the absence of toxicity symptoms in species exposed to aerial fallout versus those species where all the metal in the leaves is of soil origin.

4.3.2 Crop Plants

4.3.2.1 Metabolism: Uptake, Absorption, and Residues--

Data available on the uptake by plants of lead from natural sources are relatively sparse. Table 4.8 summarizes natural lead levels in some of the crop plants in the conterminous United States. For at least 30 years, lead added to the soil, often as an arsenate insecticide, and to air and water from automobile exhausts and industries has resulted in uptake by plant roots but only a slight increase in lead content of the stem and leaves (Lagerwerff, 1972).

Once the lead is inside the plant, it seems to be retained by cell membranes, mitochondria, and chloroplasts. Sabnis, et al., (1969) found a nonenzymic, discrete deposition of lead, osmium, and tungsten at specific sites on the thylakoid membranes of chloroplasts in the tissue of pea tendrils (*Pisum sativum* var. Alaska). The authors found that as long as lead was in the incubation medium, the deposits were obtained irrespective of the presence or absence of ATP, Mg^{++}, or Ca^{++} in various combinations or alone. Even when plants were grown in the dark for 24 hours to eliminate the effects of photophosphorylation and any traces of endogenous ATP or when lead was added to the fixtures used to prepare the tissues for electron microscopy, the deposits were still visible. Malone, et al., (1974) exposed corn plants to lead in a hydroponic solution either as a citrate or an EDTA chelate or as $PbCl_2$ or $Pb(NO_3)_2$. Light and electron microscopic studies showed that the roots generally accumulated a surface lead precipitate and slowly accumulated lead crystals in cell walls. Lead taken up by the roots was concentrated in dictyosome vesicles which fused with one another to encase the lead deposit. Movement of the lead deposits toward the outside cell wall resulted in the lead being finally localized in the cell wall outside the plasmalemma. Similar deposits were observed in stems and leaves, suggesting that lead was transported and deposited in a similar manner.

Oats (*Avena sativa*) and lettuce (*Lactua sativa* var. Black-seeded Simpson) grown in soils with a stable isotope tracer showed about the same lead concentration associated with the diffuse roots as in the soil, while in leaves the concentration of lead derived from soil uptake was only 0.5 to 30 percent as much (Rabinowitz, 1972). The author examined lettuce grown in the Salinas Valley, Southern California, and found 3 to 25 ppm lead; he viewed the excess as being due to airborne lead absorbed by the leaves. Expressed on a fresh-weight basis the lettuce contained 0.15 to 1.5 ppm lead, about the average for food which is about 0.3 ppm. John (1972)

Table 4.8 NATURAL LEAD LEVELS IN THE ASH OF CROP PLANTS[a]

Sample and Collection Locality	Observed Range, ppm	Mean, ppm
Asparagus; Wisconsin	25 - 300	87
Bean, lima; Georgia	<10 - 50 <10 - 50	<10 <10
Bean, snap; Georgia	<10 - 70 <10 - 30	<10 <10
Beet, red; Wisconsin	<10 - 25	<10
Blackeyed peas; Georgia	<10 - 70	<10
Cabbage; Georgia	<10 - 20	<10
Carrot; Wisconsin	<10 - 25	<10
Corn; Georgia	<10 - 70	7.1
Corn; Missouri		
Floodplain forest	<20 - 50	<20
Glaciated prairie	<20 - 30	<20
Corn; Wisconsin	<10 - 150	<10
Onion; Wisconsin	<10 - 25	<10
Potato; Wisconsin	<10 - 50	<10
Tomato; Georgia	<10 - 300	<10

[a] Adapted from Connor and Shacklette (1975).

found that the lead content of lettuce and oats was related to soil lead and other soil properties including pH, extractable aluminum, and total nickel. When 500 ppm lead (as lead nitrate) was added to the soil, the lead content of lettuce averaged 54 ppm while that of oat shoots and oat roots averaged 20 and 57 ppm, respectively.

Miller, et al., (1975) found that uptake of lead into shoots of 6-week-old corn plants decreased with an increase in soil pH, cation exchange capacity, and available phosphorus. Maximum accumulation of lead occurred at the 2,000-ppm lead chloride treatment level. According to MacLean, et al., (1969), the lead content of oats and alfalfa grown in four soils pretreated with $PbCl_2$ (0 to 1,000 ppm) varied inversely with the organic matter content and pH of the soils. The amount of lead taken up was reduced upon addition of phosphate or lime to acid soils. The mean lead content for oat grain, oat straw, and alfalfa tops, respectively, was 0.7 to 4.3 ppm, 1.3 to 9.8 ppm, and 1.5 to 8.5 ppm.

Corn plants, grown in sand and water with Hoagland's nutrient solution, accumulated large quantities of lead when lead nitrate was applied to the sand. When evaluating the quantity of lead accumulated, the age of the plant at the time of lead treatment was found to be very important along with the phosphate condition of the plant. The highest amounts of lead accumulated by old leaves receiving lead and in the absence of phosphate were 2,029 plus or minus 437 ppm and 936 plus or minus 78 ppm, respectively. Young leaves accumulated 11,640 plus or minus 100 ppm and 19,200 plus or minus 242 ppm in the same order (Miller and Koeppe, 1971). Baumhardt and Welch (1972) found that the lead content (ppm) of corn stover grown in a field which received lead acetate treatments of 0 and 3,200 kilograms per hectare was: 2.4 and 37.8 for whole young plants, 3.6 to 27.6 for leaves at tasselling, and 4.2 and 20.4 for whole plants at grain harvest. The lead content of grain averaged 0.4 ppm lead and was not affected by added lead.

Bazzaz, et al., (1974b) found that lead accumulation trends in corn and soybeans were similar at lower treatment levels but were slightly different at higher levels. The uptake by corn increased sharply as the amount of lead chloride in the growth medium increased. Maximum accumulation of about 450 ppm occurred at a medium concentration of 1,000 ppm. The maximum accumulation for soybeans was 151 ppm grown in a medium with the same lead concentration. Lagerwerff, et al., (1973) grew corn and alfalfa plants in potted Chester silt loam at two soil pH levels (5.2 and 7.2) and with HCl-extractable soil lead (as $PbCl_2$) levels of 12, 64, 113, and 212 ppm. Most treatments were carried out in a greenhouse where the plants were exposed to aerial lead from nearby traffic as well as leaded-paint particulates from the greenhouse windows. No clear relationship was established between uptake and soil lead content in the leaves and stalk of the upper section of corn. In the lower section lead content in the leaves and stalk increased from 53 to 110 ppm, and from 4.6 to 12.5 ppm, respectively, as the soil content increased from 12 to 212 ppm lead at pH 5.2. As the extractable lead content of the soil increased from 12 to 212 ppm, the differences between rinsed and unrinsed samples of the first clipping of alfalfa tops increased from 1.6 to 9.5 ppm, and from 3.2 to 4.9 ppm lead on a dry-weight basis at soil pH 5.2 and 7.2, respectively. A similar trend was shown with the second clipping. Page, et al., (1971) found that alfalfa plants lost 50 percent of their lead by rinsing once with water.

Corn plants grown on soil treated with municipal sludge for 35 years did not show an appreciable accumulation of lead in the grain as compared to control crops (Kirkham, 1975). In general, the roots, stems, leaves, and husks had much higher lead concentrations than those of control plants. The lead concentration in roots was 540 ppm compared to less than 5 ppm in grain. The concentration of lead and other metals in the grain of sludge-treated plants was not greater than that in grain from control plants. These data show that very little lead was translocated to the above-ground portions even in sludge-amended soils. In contrast, Anderson and Nilsson (1972) noted a 50 percent increase in extractable soil lead and the lead content of vegetation (5.2 ppm, background level; 7.7 ppm, sludge added) when sewage sludge (containing 293 ppm lead) was used as a plant nutrient source on cultivated soils.

The uptake of metals by seven vegetable crops (carrots, lettuce, peas, potatoes, radishes, sweet corn, and tomatoes) after 0, 102, 205, and 450 tons per hectare of sewage sludge was applied to coarse, sandy soil was studied by Dowdy and Larson, (1975b). Lead uptake was insignificant and did not exceed 1.0 ppm in the root and tuber tissue, although 230 kilograms lead per hectare was added. The low values (less than 1 ppm) contrast with values of 20 to 25 ppm lead in radish roots (Lagerwerff, 1971) grown on soil containing 70 to 370 kilograms lead per hectare. The edible fruiting tissue had little or no increase in the iron, manganese, copper, lead, and boron contents with applications of sludge. The data indicate, in this case, that lead-containing sewage sludge added to soil does not significantly affect tissue-lead content.

In those instances where lead toxicities to animals and humans have occurred, the sources of lead in the foods and feeds were not due to plant absorption from soils but were caused by contamination during processing, storage, or deposition from lead in air onto plant surfaces (Page, 1974; see Sections 5.5 and 8.3.1). Menzies (1974) points out that lead is generally inactivated in sludge by being tied up with phosphorus. This accounts in part, for the insignificant amounts of lead that are usually absorbed by plants growing on sludge-amended soil. Furthermore, lead or other trace element levels in higher plants grown on sludge-amended soils are dependent on the amount of sludge applied, composition of the sludge, soil pH, and plant species.

John and VanLaerhoven (1972a) grew oat seedlings and lettuce in silty clay loam soil that received lead (as $PbCl_2$), lime, and nitrogen treatments. Lettuce leaf lead content (140.6 ppm) was highest at the 1,000-ppm treatment level. When soil was limed, only small increases were found. In oat tops lead increased from 3.2 to 57.4 ppm as a result of adding 1,000 ppm lead to unlimed soil whereas the corresponding increase for limed soil was only from 5.6 to 16.8 ppm. Oat root lead content was not significantly affected. When lead and nitrogen were added simultaneously, the lead content of both plant species varied depending on the source of lead and rate of nitrogen applied. Application of low levels of nitrogen reduced uptake of lead by lettuce and oat roots only.

Cox and Rains (1972) tested liming at 0, 2, and 4 metric tons per nectare (0, 3.6, and 7.1 tons/acre) as a means for reducing lead uptake by five plant species (Glycine max, Triticum aestivum, Trifolium subterraneum, Zea mays and Avena sativa) from two lead-contaminated soils. 2 and 4 metric tons lime per hectare reduced lead concentrations in the tops of 10-week-old plants of all species. Uptake was decreased by lime simply because of lower availability of soil lead. At maturity, Glycine max growing in soil limed at the rate of 0 to 1.8 metric tons (0 to 2 tons) per acre, accumulathe the following amounts of lead: 37.2 to 36.8 ppm (seed pods) and 62.3 to 25.3 ppm (seeds) in the 0- to 10-cm soil horizons, and 30.4 to 23.7 ppm (seed pods) and 60.4 to 27.6 ppm (seeds) in the 10- to 30-cm soil horizons.

Lagerwerff (1971) grew radish plants in an open field 200 meters from traffic and in a growth chamber located in a windowless room to determine uptake of cadmium, lead, and zinc by radish from soil and air. A tenfold increase in the lead content of soil was reflected in an increase in the lead content of radish by a factor of less than two. The tops and roots of radish grown inside on a low lead content soil of pH 5.9 already had 13.3 and 19.4 ppm lead on a dry-weight basis, respectively. The highest lead content in radish roots grown outside at pH 5.9 was about 119 ppm; at pH 7.2, the content was about 89 ppm. Radish tops grown outside accumulated approximately 148 ppm at pH 5.9 and about 85 ppm at pH 7.2

Ter Haar, et al., (1969) grew radishes in specially-constructed growth chambers with normal (0.96 microgram Pb per cubic meter) or filtered air (0.3 microgram Pb per cubic meter) while either distilled or lead-containing water (40 micrograms Pb per liter as $PbCl_2$) was applied to the leaves or soil surface. The concentration of lead in radish leaves grown in filtered air was 2.3 ppm; in unfiltered air, 2.7 ppm; with distilled water, 2.7 ppm; with lead-containing water, 2.2 ppm; under foliar application of water, 2.2 ppm; and under soil application of water, 2.7 ppm. The lead content of the hypocotyls grown in filtered air was 2 ppm; in unfiltered air, 1.8 ppm; in distilled water, 2 ppm; in lead-containing water, 1.8 ppm; under foliar application of water, 1.5 ppm; and under soil application, 2.3 ppm.

Dedolph, et al., (1970) obtained essentially the same results as did Ter Haar, et al., (1969) using filtered air with a lead content of 0.09 microgram per cubic meter and unfiltered air containing 1.45 micrograms per cubic meter. Radishes were grown in field plots 12.2, 36.6, and 155 meters (40, 120, and 510 feet) from the road under the following conditions in the order given: 82, 45, and 27 ppm, soil lead content and an atmospheric lead concentration of 2.32, 1.71, and 1.07 micrograms Pb per cubic meter in the air. Lead content (ppm) of radish leaves was 16.4, 10.8, and 2.8 and that of radish roots was 0.7, 0.8, and 0.8, respectively, under the conditions cited above. Ter Haar (1970 and 1973) grew several food crops in greenhouses supplied with filtered and ambient air and in plots planted perpendicular to a busy highway. Inedible portions of the plants, bean leaves, corn and soybean husks, and oat, wheat, and rice chaff showed a two- or threefold increase in lead concentration when grown near the road or in the greenhouse with unfiltered air. Tables 4.9 and 4.10 summarize the results obtained.

John and VanLaerhoven (1972b) studied lead uptake by seven food crops (leaf lettuce, spinach, broccoli, cauliflower, oats, radishes and carrots) in a growth chamber experiment which involved three rates of $PbCl_2$ soil applications. Lettuce and spinach leaves and the tuberous portions of radish and carrot plants accumulated markedly higher lead concentrations than did the edible portions of the three other plant species. In all plants parts, lead concentrations increased as more lead was added to the soil. Differences among lead concentrations in tissues of these plants were most evident with the high lead treatment, 1,000 milligrams lead per kilogram. Concentrations in root portions ranged from 396.6 to 867.7 milligrams lead per kilogram and increased with the following sequence of plant species: oats, cauliflower, carrots, broccoli, and lettuce. Among the above-ground plant parts, lettuce and spinach leaves, with 54.2 and 39.3 milligrams lead per kilogram, respectively, contained approximately twice the lead levels found in any other aerial portion. The least lead concentration was found in oat grain.

Motto, et al., (1970) grew five crops (carrots, corn, lettuce, potatoes, and tomatoes) at three distances from highways in New Jersey having various traffice densities. The same crops were grown in the greenhouse with soil from the surface 15.2 centimeters (6 inches) of field plots and in acid-washed sand to which soluble lead was added. Analysis of plants grown in the field revealed that the highest lead levels were associated with leaves; lower levels were in the roots. These same plants grown in the greenhouse exhibited lower levels in the leaves relative to the roots. The overall results, as summarized in Tables 4.11 and 4.12, showed that the lead content of plants and soils increased with increasing traffic volume and decreased with increasing distance from highways. Most of the lead accumulation was within 30.5 meters (100 feet) of highways. The edible portion of carrots, corn, potatoes, and tomatoes contained the lowest amounts of lead and showed the least effect of increased lead supply. Edible portions of lettuce contained a larger amount of lead.

Page, et al., (1971) ascertained the lead content of 27 varieties of consumer crops and plants growing near some major southern California highways. The data, too voluminous to repeat here, cover the effects of distance from the highway, and the effect of washing on the lead content of both edible and inedible portions of the plants. Exposed tissues of plants grown very close to major highways contained more lead than similar tissues of plants grown some distance from highways. Beyond 150 meters lead in or on vegetation was no longer related to distance from the highway and appeared to be governed by regional effects as opposed to local effects. Exposed tissues of plants with flexible, rough, hairy surfaces, and close to highways accumulated more lead per unit time than did those with smooth surfaces. Duration of exposure was found to be important. Tomatoes, for example, picked at various stages of maturity, showed increased lead as the season progressed. Lead in parts of plants not in direct contact with the atmosphere such as root, pod,

TABLE 4.9. LEAD IN CROPS, GREENHOUSE STUDIES[a] (micrograms per gram dry weight)

	Unfiltered Air	Filtered Air	LSD[b]
Air	1.45 $\mu g/m^3$	0.09 $\mu g/m^3$	–
Soil	17.1	17.1	–
Leaf lettuce	6.6[c]	3.2	1.3
Cabbage head	1.0	1.1	0.35
Cabbage–unharvested leaves	4.5	5.8	1.6
Tomatoes	0.59	0.72	0.26
Beans	1.4	1.2	0.52
Bean leaves	20.9[c]	7.9	8.8
Sweet corn			
Kernel	0.22	0.27	0.22
Cob	0.43[c]	0.69	0.24
Husk	6.9[c]	1.8	1.5
Carrots	1.7	2.1	1.9
Potatoes	0.30	0.33	0.12
Wheat	0.18	0.16	0.06

[a] Source: Ter Haar. Reprinted with permission from Environmental Science and Technology. (c) American Chemical Society, 1970.

[b] Least significant difference.

[c] Different from other values in row at 95 percent level of confidence.

TABLE 4.10 LEAD IN CROPS, HIGHWAY STUDIES[a]
(micrograms per gram dry weight)

	Feet from Road			
	30	120	520	LSD[b]
Air	2.3^{c} $\mu g/m^3$	1.7^{d} $\mu g/m^3$	1.1 $\mu g/m^3$	–
Soil	65^{c}	40^{d}	25	–
Leaf lettuce	6.5	5.0	4.8	3.1
Cabbage head	0.56	0.86	0.83	0.44
Cabbage–unharvested leaves	6.4^{c}	8.9^{d}	4.0	1.3
Tomatoes	1.3	1.2	1.6	1.3
Beans	1.9^{c}	1.2	0.90	0.47
Potatoes	0.48	0.64	0.40	0.27
Sweet corn				
Kernel	0.39	0.21	0.83^{c}	0.31
Cob	0.74	0.55	0.68	0.21
Husk	12.6^{c}	6.6	5.7	3.6
Soybeans				
Beans	0.28^{c}	0.12	0.10	0.10
Husk	15.9^{c}	8.0^{d}	5.3	0.22
Oats				
Kernel	0.47	–	0.53	0.37
Chaff	31.4^{c}	15.5	12.8	15.5
Carrots	1.6	–	1.5	0.61
Wheat				
Kernel	0.62	0.42	0.48	0.17
Chaff	17.8^{c}	9.8^{d}	6.2	1.6

[a] Source: Ter Haar. Reprinted with permission from Environmental Science and Technology. (c) American Chemical Society, 1970.

[b] Least significant difference.

[c] Different from others at 95 percent level of confidence.

Table 4.11 CONCENTRATION OF LEAD IN FIVE CROPS GROWN AT THREE FIELD SITES IN 1968[a]

	Traffic Volume								
	12,500 Cars per 24 hr			**47,100 Cars per 24 hr**			**49,000 Cars per 24 hr**		
Distance from highway, ft	30	100	250	30	100	250	30	100	250
Air lead, $\mu g/m^3$	1.4	1.1	1.0	4.5	2.7	2.4	5.2	3.3	2.5
Soil lead, ppm at 0–6 in.	54	38	33	134	138	300	229	130	89
Lead content, ppm, of:									
Carrot									
Tops	18	11	14	37	26	21	53	22	17
Roots	3.8	5.3	3.9	6.2	9.5	9.4	9.1	10	5.0
Corn									
Tassel	31	7.4	7.8	179	144	69	–	–	–
Leaves	19	17	14	86	47	36	88	51	40
Stalk	3.6	3.7	0.9	5.6	3.6	0.2	6.2	3.4	3.6
Husk									
Outer	11	5.0	6.8	3.0	5.0	2.6	–	–	–
Inner	5.0	5.2	2.4				–	–	–
Roots	6.0	3.9	5.4	19	14	19	54	19	–
Kernel	3.8	3.6	3.1	0.0	0.2	0.2	–	–	–
Cob	8.0	3.2	2.6	0.4	0.0	0.4	–	–	–
Lettuce									
Leaves	12	13	–	24	21	14	56	35	–
Roots	16	15	–	24	27	39	61	32	–
Potato									
Leaves	36	31	21	87	47	29	–	–	–
Stems	12	8.4	7.8	15	11	14	–	–	–
Roots	22	23	18	33	49	58	–	–	–
Tuber	0.5	1.5	1.0	2.6	3.0	3.0	–	–	–
Tomato									
Leaves	36	25	17	76	82	40	88	52	44
Stem	9.0	9.8	6.9	27	25	31	29	13	7.7
Root	11	15	14	27	35	50	37	12	9.6
Fruit	2.8	3.0	2.4	4.6	2.7	2.8	3.6	1.2	3.2

[a] Source: Motto, et al. Reprinted with permission from Environmental Science and Technology. (c) American Chemical Society, 1970.

Table 4.12 LEAD CONTENT OF PLANTS GROWN IN GREENHOUSE IN 1963[a]

	Soil (ppm 0-15 cm)			Sand Treatment (ppm Pb)			
	164	95	76	0	1	2	4
	Pb, ppm						
Carrot							
Tops	18	14	...	8.7	16	19	27
Roots	16	6	9	3.1	7.9	18	21
Corn							
Tassel	24	...	...	7.8	8.1	7.4	9.2
Leaves	74	18	...	11	19	39	88
Stalk	5.2	3.9	...	0.6	11	28	44
Husk	17	4.1	4.9	...	...	...	...
Outer	...	...	...	2.9	7.9	15	23
Inner	...	...	...	3.9	7.3	13	16
Roots	14	4.7	10	3.7	12	22	35
Kernel	1.3	1.6	2.1	1.0	1.7	2.8	3.3
Cob	1.2	1.1	1.7	2.4	2.7	4.3	10
Lettuce							
Leaves	8.7	7.6	6.9	5.7	12	16	37
Roots	94	11	12	7.6	108	182	332
Potato							
Leaves	41	31	33	11	7.8	12	12
Stems	39	16	13	7.6	29	55	123
Roots	...	...	...	30	200	451	764
Tuber	6.2	3.7	3.7	1.0	0.6	2.6	1.2
Tomato							
Leaves	25	18	19	8.1	8.1	15	16
Stem	13	4.7	4.2	3.6	24	89	87
Root	51	13	13	17	418	690	739
Fruit	3.6	3.4	3.5	3.6	2.5	2.3	2.1

[a] Source: Motto, et al. Reprinted with permission from Environmental Science and Technology. (c) American Chemical Society, 1979.

and husk crops was not substantially influenced by proximity to highly traveled roads. Corn kernels, lima beans, and carrots, and sugar beet roots all contained comparatively small amounts of lead which were not significantly related to distance from the highway.

One hundred thirty-two samples of a variety of fruits and vegetables grown near heavily traveled highways primarily in California were analyzed for lead. The concentrations of the lead residues are summarized in Table 4.13 (Kleinman, 1968).

4.3.2.2 Effects--

Holl and Hampp (1975) in reviewing the literature on lead and plants cited the few cases in which lead was found to increase plant growth or yield. Lead increased the yield of barley, corn, wheat, buckwheat, and other crop plants as well as sugar yield from sugar beets while the tuber mass and starch content of potatoes decreased. Baumhardt and Welch (1972) found that corn grain yields were neither decreased nor enhanced by additions of lead acetate to soil. Yields with added lead were 96 to 103 percent as great as yields from controls. The data showed that lead additions as high as 3,200 kilograms per hectare had no effect on grain yield of corn. Lagerwerff, et al., (1973) found that total corn yield was not significantly affected by liming the soil or amending the soil with graded amounts of lead chloride. With alfalfa, yield was only affected by soil lead concentration when the soil was limed.

Garber (1974) subjected various agricultural and garden plots to varying quantities of lead-containing fly dusts typical of foundry operations and observed the effects on growth and yield. Lead had a strong, inhibiting effect on the growth and pod yield of bush beans. Bean plants at the highest lead concentration (10,000 ppm) had leaves which were only half as well developed as those of control plants, and which showed reddish-brown mottling along the leaf veins as well as a strong chlorosis in newly-formed leaves. The number of nodules on the roots exposed to 2,000 ppm lead was small, while at 10,000 ppm lead, no nodules were formed. Tomatoes, bean sprouts, and lettuce showed a yield reduction when treated with 120 grams of lead-containing dust per square meter. Potatoes, in contrast, increased yield at the higher treatment level. Considerable yield reductions were also found for peas, lettuce, and carrots in loamy sand soils. John and VanLaerhoven (1972a) found that lead application (1,000 ppm Pb singly as $PbCl_2$, $PbCO_3$ or $Pb(NO_3)_2$ or in combination) reduced lettuce yield significantly whereas yields of oat top growth and roots were not affected. The interaction between lime and lead treatments had a significant effect upon yields of lettuce and oat shoots, but had no effect on yield of roots. Liming reduced lead uptake by above-ground plant portions to a much greater degree than by oat roots.

Great variations in lead sensitivity of various cultured grasses have been demonstrated. *Zea mays* (maize) and *Secale cereale* (rye) were not sensitive to lead acetate concentrations of 10^{-10} to 100 milligrams of lead per liter. Barley, oats, and especially wheat showed damage symptoms even

Table 4.13 LEAD CONTENT OF FRUITS AND VEGETABLES CORRELATED WITH DISTANCE FROM TRAFFIC AND TRAFFIC LOAD[a]

Crop Plant	Distance from Highway[b]	Traffic Load[c]	Growth Period, weeks	Highest Average Value for lead Content, ppm
Grapefruit	1	M	13	0.08
Oranges	3	M	13	0.12
Lemons	2	H,L	12-16	0.18
Cantaloupe or honeydew	1	L	7-8	0.16
Strawberries	3	H,L	22	0.15
Collards	3	M	12	0.90
Lettuce	2	M	12-14	0.26
Endive	3	M,L	12	0.05
Spinach	2	L	28	0.27
Broccoli	2	H,M,L	8-12	0.30
Cabbage	1	M,L	8-27	0.03
Turnip greens	3	H	18	0.31
Rape	3	H	13	0.25
Tomatoes	3	H,M,L	12	0.05
Pole beans	2	L	12	0.12
Potatoes	1	M	10	0.02
Carrots	1	M,L	12	0.09
Radishes	2	L	8	0.06
Celery	3	M	26-28	0.16
Cauliflower	3	H	8-12	0.03

[a] Modified from Kleinman (1968).

[b] 1 = 9 to 22.9 meters (0 to 25 yards); 2 = 22.9 to 229 meters (25 to 250 yards); 3 = above 229 meters (250 yards).

[c] H = Heavy; M = Medium; L = Light.

at low lead concentrations. There was visible damage to Hordeum vulgare (barley) 4 days after exposure to 0.1 M $Pb(NO_3)_2$, ending in death (Holl and Hampp, 1975).

Baumhardt and Welch (1972) found that corn grown in a field to which lead acetate concentrations of 0 to 3,2000 kilograms of lead per hectare had been added showed no effect in terms of emergence and plant height. Neither were any morphological, color, maturity nor other growth differences visually observed during a 2-year study. Miller, et al., (1975) found that lead and cadmium together inhibited corn root elongation, but not individually. Soil properties were not found to be directly related to the effects of lead and/or cadmium although the greatest reduction of growth was seen in low cation exchange capacity (CEC) and low pH soils. According to Miller and Koeppe (1971), as little as 24 ppm lead as $PbCl_2$ in sand culture caused a stunting of growth of corn plans under phosphate-deficient conditions.

Phaseolus vulgaris (bean) plants were visibly damaged as soon as 30 minutes after exposure to a concentration of 33,000 ppm lead nitrate. There was a loss of turgor pressure and death after 24 hours. A lead concentration of 3.3 ppm enhanced growth activity whereas the limiting concentration which caused no damage or growth stimulation was 330 ppm. Leaves not fully differentiated at the beginning of lead exposures were chlorotic. Phaseolus was damaged by 30 ppm lead as the sulfate alone, or in combination with other nutrient salts in solution culture. No increase in toxicity from 0 to 30 ppm was detected. Lead nitrate and acetate in concentrations exceeding 100 ppm reduced the germination of cress and mustard seeds and retarded subsequent growth, to concentrations of 1,000 to 2,000 ppm completely inhibited seed germination (Holl and Hampp, 1975; Zimdahl and Arvik, 1973). These authors also indicated that high lead concentrations inhibit root growth considerably. Remarkably thick roots with abnormally long root hairs were observed on cereals after lead treatment. In contrast, an abnormal thinning of roots accompanied by a reduction of root hair numbers has also been reported. A 93 percent inhibition of root ontogeny of germinating lettuce seeds was observed at a lead concentration of 330 ppm.

An inhibition of mitosis accompanied by reduced growth was observed in Allium cepa (onion) and Zea mays (maize) when the nutrition solutes contained rising quantities of lead. Differentiating young plant tissues have been found to be much more sensitive to lead than mature tissues (Holl and Hampp, 1975). Radu (1971) found that the lead ion at a concentration of at least 6 ppm is a mitotic poison. Experiments conducted with Allium cep (onion) and Vicia faba (vetch) in vivo using lead nitrate resulted in altered mitotic figures. Stathmokinetic effects were elicited. Higher lead concentrations induced chromosomal modifications. According to Levan (1945), mitosis in onion root tips induced by lead nitrate has been found to be indistinguishable from that induced by colchicine in terms of spindle disturbances and chromatid formation. Ahlberg, et al., (1972) subjected an exposed clone of onion bulbs to varying concentrations of alkyl lead compounds. Disturbances of the miotic spindle fiber mechanism occurred at even very low concentrations (10^{-6} and 10^{-7} M). The ethyl compounds exerted a stronger effect on the spindle fiber mechanism than the methyl compounds. Applying the highest dosage, a strong inhibition of mitosis was noted with triethyllead and trimethyllead after 6 and 24 hours of treatment, respectively. Small, but significant increases of chromosome bridges and fragments as well as micronuclei were observed with triethyllead concentration of at least 10^{-5} M. The trimethyllead compounds did not produce a corresponding effect. Barker (1972) grew explanted tissues of cauliflower, lettuce, potato and carrot on media containing varying concentrations of lead acetate. Lettuce was responsive to lead at 0.5 ppm and the growth of carrot explants was significantly slowed at 0.005 ppm and drastically hampered at 5 ppm. Toxicity to the growth of cauliflower and potato was noted between 0.5 and 5 ppm. None of the tissues showed discoloration or other gross morphological abnormalities.

Hampp and Lendzian (1974) found that the syntheses of both types of chlorophyll in 16-day-old oat seedlings was reduced in proportion to increasing amounts of lead ions. Concentrations as low as 50 micromoles (14 ppm) $PbCl_2$ had a statistically significant effect. 0 to 500 micromoles inhibited chlorophyll b syntheses to a greater extent than that of chlorophyll a. At higher concentrations the ratio of chlorophyll a to chlorophyll b tended toward unity.

A pronounced inhibition of transpiration and water uptake in spinach leaves was demonstrated in the presence of less than 100 micromoles Pb(II). A rise in lead concentration [exceeding 100 micromoles Pb(II)] however, was not accompanied by a proportional increase of inhibition. There was a pronounced inhibition of gas turnover when 25 micromoles of lead were applied. There was a greater inhibition of CO_2 uptake in the light period than of CO_2 release in the dark period. The intensity of $^{14}CO_2$ fixation by isolated spinach chloroplasts was reduced by all lead concentrations tested (2 to 200 micromoles lead nitrate). ATP syntheses in illuminated chloroplasts was also reduced (Holl and Hampp, 1975). Corn (Zea Mays) and soybean (Glycine max) plants grown in media receiving lead treatments of showed decreased net photosyntheses and transpiration at increased treatment levels. Treatment included application of solutions containing 0, 250, 500, 1,000, 2,000 and 4,000 ppm lead in one liter of solution providing 0, 15.6, 31.3, 62.5, 125 and 250 milligrams of lead per plant. Sixteen individual trays of seedlings of corn and soybeans were used. At 250 milligrams of lead per plant photosyntheses was only 10 percent of maximum in soybeans, but 47 percent in corn although the tissue lead content was much higher than that of soybeans. Transpiration exhibited similar trends to photosynthesis (Bazzaz, et al., 1974b).

Lead significantly affects the photosynthesis process in plants. In fact, photosynthesis is more sensitive to lead than the respiration apparatus. Miles, et al., (1972) report that lead salts (chloride) inhibited electron transport in Photosystem II of the chloroplasts in spinach (Spinacia oleracea) and tomato (Lycopersicum esculentum) leaves as contrasted to that in Photosystem I. Holl and Hampp (1975) report a case in which Photosystem I in spinach chloroplasts was inhibited in the presence of lead ions. The inhibition was less pronounced than that for Photosystem II. Bazzaz and Govindjee (1974) found that lead chloride inhibits or stimulates Photosystem II activity depending on the pH of the reaction media. At pH 7.8, an inhibition of 16 to 39 percent with 0.75 to 9 millimoles $PbCl_2$ was observed;

however, a stimulatory effect of 20 percent was observed with 9 millimoles $PbCl_2$ at pH 6.5. Light intensity was 2×10^6 ergs cm^{-2} sec^{-1}. One ml samples containing 5 to 8 micrograms chloroplast were suspended in buffer and 50 micromoles 3 - (3, 4-dichlorophenyl) 1, 1-dimethylurea.

In spinach root and leaf homogenates, several enzymes unique to the photosynthetic process exhibited changes in activities in the presence of 5 to 200 micromoles of lead nitrate (Holl and Hampp, 1975). Five micromoles of lead nitrate inhibited ribulose diphosphate carboxylase, and lactate dehydrogenase showed a similar but less pronounced decrease in activity. Pyruvate kinase activity was enhanced by all lead nitrate concentrations tested, reaching an optimum at 20 micromoles. The NAD- and NADP-dependent triose phosphate dehydrogenase systems were mostly activated at the respective lead concentrations of 100 to 500 micromoles and 100 to 1,100 micromoles. In plant tissues, lead ions have been found to lower the concentrations of metabolites such as acetyl coenzyme A, malic acid and other soluble organic acids, and kardenolides.

Koeppe and Miller (1970) and Miller and Koeppe (1971) have found that lead affects mitochondrial respiration. In corn mitochondria, lead chloride (10 to 62 micromoles per liter) stimulated the oxidation of exogenous, reduced NADH by 174 to 640 percent whereas 12.5 micromoles per liter of lead chloride inhibited succinate oxidation by more than 80 percent. When inorganic phosphate was included in the reaction media, the subsequent addition of lead was not effective due to the low solubility of lead phosphate. When the addition of lead was followed by the addition of phosphate, succinate oxidation inhibition was released but there was no reduction in the stimulation of oxidation of NADH. It was therefore concluded that high concentrations of lead in plants will not be effective due to the precipitation of lead if sufficient phosphate is present.

4.3.3 Translocation in Vascular Plants

Contaminant movement within vegetation depends on soil-plant-water relations. Luxmoore, et al., (1975) coupled an atmosphere-soil-plant-water relations model with a plant growth and uptake model to describe the two pathways for contaminant movement in vegetation: water movement from roots to leaves and sugar translocation from leaves to roots. Most of the lead studies, though limited in number, indicate that lead is either unavailable to the plant or is "fixed" in the roots and only small amounts are translocated to the above-ground parts of the plant even when the plants are grown on soil containing substantial amounts of lead. This is due not only to the solubility of lead in the soil but to some internal factors which govern the mobility of lead within the plant. This phenomenon varies among plant species (Hemphill, 1972; MacLean, et al., 1969; Marten and Hammond, 1966; Mitchell and Reith, 1966; Rabinowitz, 1972; Rolfe, 1973; Rule, et al., 1975). Significant increases in lead content of top growth due to soil application of lead have been reported by Jones and Hatch (1945) and Warren and Delavault (1962).

Banus, et al., (1974) have found that lead is rapidly transported from salt marsh sediments to the leaves and shoots of marsh grasses, especially those of cordgrass (Spartina alterniflora). It was previously thought that grass roots were very effective barriers of the movement to lead to other parts of the plant. Jones and Clement (1972) and Jones, et al., (1973a) studied the uptake of lead by roots and its transport to shoots using perennial ryegrass (Lolium perenne var. S23) in solution culture rather than complex soils. The proportion of lead reaching the shoots at first harvest (7 days after lead additions) was 3.5 to 22.7 percent of the total uptake, the lower value being for plants with the greatest burden. Transport to the shoots continued throughout experimental periods of 21 and 28 days, but did not exceed 28.9 percent of the total uptake. At the highest level of added lead, there was some indication that the rate of transport increased with time. The experiments showed that the roots of actively-growing ryegrass plants readily take up lead but pass only a small proportion to the shoots. In contrast, Jones, et al., (1973b) found that when perennial ryegrass is growing in soil, the roots restrict the movement of lead into the tops of high-yielding plants, but when growth is limited by a sulfur deficiency the concentration in the tops increases markedly. During the winter period when the growth rate is low, considerably increases have been observed in the lead content of grass shoots (Jones and Clement, 1972; Jones, et al., 1973a). Mitchell and Reith (1966) reported lead increases from 0.8 to 1.5 ppm in August/September to 5.1, 11.9, and 21.8 ppm in late November in ryegrass, cocksfoot, and mixed pasture grasses, respectively. The above increases were confined to the months of restricted growth. The lead was transported to the stem prior to winter dormancy possibly by the way of the phloem. This same phenomenon was found in leaves of deciduous trees and in wild oats (Rains, 1971; Zimdahl and Arvik, 1973).

Rabinowitz (1972) verified foliar absorption and subsequent translocation of lead halide aerosols by oats (Avena sativa) and lettuce (Lactua sativa var. Black-Seeded Simpson) grown near the San Diego Freeway which reportedly carried 360,000 cars per day. Four to ten parts per million of atmospheric lead was absorbed by the leaves and translocated downward in the plants to the central taproots. John and VanLaerhoven (1972a) believe that since higher levels of lead were found in oat roots than in tops, translocation of lead is of a restricted nature. Based on their findings, the authors postulated that liming may restrict the translocation of lead from roots to above-ground portions. According to a calculated transport index, there was an enhancement of lead movement into the above-ground portion of the oat plants when lead was added to the soil.

Generally, the translocation of lead in plants cannot be considered an isolated phenomenon, rather it is related to such factors as involvement of chelates, ion concentration in the medium, pH, and chemical equilibrium prevalent in the soil medium in question. The uptake can probably be controlled through modification of the soil with the appropriate minerals which affect these chemical equilibria. For example, Miller and Koeppe (1971) found that corn plants grown in a soil deficient in phosphate allowed a very substantial uptake and translocation of lead. Because of the buffering capabilities of soils and plant roots, as well as absorption and precipitation phenomena, most lead in soils is not going to be translocated to above-ground regions of plants. However, uptake can be appreciable following alterations in the environmental state of the plant as well as the physiological condition of the plant.

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5.0 EFFECTS ON ANIMALS

5.1 SUMMARY

Much evidence exists for elevated amounts of lead residues in wild animals as a result of environmental pollution from a variety of lead sources. In aquatic systems, both freshwater and marine, a variety of benthic and pelagic organisms including worms, mollusks, and fishes, accumulate lead; in some cases these levels exceed the "norm" or baseline level for the particular organism. However, excluding grossly polluted streams associated with some mining operations, that lead is deleterious to aquatic populations and communities in nature has not been demonstrated. Numerous laboratory investigations of short-term and chronic effects of lead on fishes have been made. The behavior of lead in aquatic systems, and thus the availability of lead to the biota, have not been resolved. It is generally believed that lead is precipitated from the water column to bottom sediments, remaining there with little effect on or translocation to the aquatic flora and fauna. However, there is recent evidence that methylation of inorganic lead can occur in an aquatic environment. This may eventually be shown to be significant.

Biotranslocation and magnification of lead in certain components of terrestrial ecosystems have been demonstrated. In areas of high lead emission from automobile exhaust, predaceous insects were found to have higher lead levels than those insects which fed upon plants. This indicates a biomagnification of lead from herbivore to carnivore trophic levels.

Lead poisoning remains a serious health problem in waterfowl, especially for mallard ducks. Lead shot from spent shotgun shells is the source of poisoning. Evidence obtained from starling and pigeon populations suggests that lead residue levels in nongame birds are higher in urban areas.

Poisoning of domestic animals - cattle, horses, and pets - is most frequently attributable to ingestion of lead contained in lead-based paints, linoleum, storage batteries, putty, and used motor oil. Airborne lead from mining, smelting, and lead-using industries has poisoned cattle and horses in localized areas by contaminating hay and pasturage. Airborne lead from vehicular exhaust emission is suspected in one instance of causing lead poisoning in zoo animals. Small, wild mammals which inhabit areas adjacent to major highways have elevated body burdens of lead.

5.2 INVERTEBRATES

Because of the importance of invertebrates as components of food chains providing food sources for a large number of organisms occupying higher trophic levels, the uptake, accumulation, and toxicity of lead have been studied in a variety of invertebrate species.

5.2.1 Aquatic

5.2.1.1 Metabolism: Uptake, Absorption, and Residues--

Drifmeyer and Odum (1975) investigated the uptake of lead, zinc, and manganese by salt-marsh biota living in two diked, dredge-spoil disposal areas in Virginia which had received heavy metal-containing dredge-spoil. Eighty-two specimens of the grass shrimp (*Palaemonetes pugio*) showed a significant (0.01 confidence level) difference in whole-body lead contents between grass shrimp collected from ponds inside diked, spoil-disposal areas where lead levels averaged 11.0 plus or minus 1.8 ppm, and grass shrimp from natural marsh areas where the concentration of lead averaged 0.2 plus or minus 0.3 ppm.

Warnick and Bell (1969) studied the acute toxicity of lead in three species of aquatic insects. Individuals that were killed in these static tests absorbed 0.05, 0.12, and 0.08 mg of lead, respectively, for *Acroneura* (stonefly), *Ephemerella* (Mayfly), and *Hydropsyche* (Caddisfly).

Gale, et al., (1973) found that lead levels in consumer organisms in Missouri's New Lead Belt decreased as the distance from tailings ponds increased. At distances of 0.3 to 6.7 kilometers (0.2 to 4.2 miles) downstream from a tailings pond which holds combined mine and mill effluents, lead levels in crayfish and snails were 69 to 28 ppm, and 116 to 39 ppm dry weight, respectively. These levels approach background values at 8 to 9.7 km (5 to 6 miles) downstream.

Shells of the freshwater clam *Corbicula manilensis* are considered good monitors of total lead increase over baseline concentrations in water at pH 7 or above (Clarke and Clarke, 1974). Empty *Corbicula* shells were collected from the Harpeth River in Nashville, Tennessee. One group was analyzed for their lead content while others were placed in 70 liters of lead-spiked [16 ppm $Pb(NO_3)_2$], deionized water or 70 liters of deionized water buffered at pH 8.38 for 3 months. Those shells analyzed without further experimentation had an average lead content of 1.9 ppm. Those exposed to lead-spiked, deionized water and to lead-free, deionized water had average lead concentrations of 69.5 and 4.1 ppm, respectively. Clam species from the Illinois River which had an average concentration of 28 ppm of lead in bottom sediments were found to contain the following amounts of lead (averages in parentheses): *Fusconaia flava*, 1.8 to 5.1 (3.7) ppm; *Amblema plicata*, 1.1 to 7.5 (2.7) ppm; and *Quadrula quadrula*, 0.9 to 3.8 (2.2) ppm (Mathis and Cummings, 1973). These same authors reported 6 to 39 ppm lead (17 ppm, average concentration) for the tubificids *Limnodrilus hoffmeisteri* and *Tubifex tubifex*.

The uptake of heavy metals from seawater or estuaries by the animal living therein may occur on the body surface, across the general body surface, or on specialized areas such as the gills or the shell. Bryan (1971) indicated that lead, zinc, and cadmium are stored in the hepatopancreas (digestive gland) of the clam *Scrobicularia plana* and in the renal organs of the scallop, *Chlamys opercularis*. Anderlini (1974) analyzed the gills, mantle, digestive gland, and foot of 74 specimens of the red abalone from five sites on the California coast for eight heavy metals. Lead concentrations were below detection (less than 0.1 ppm, dry weight) in the gills, mantle and foot. Highest concentrations of lead were in the digestive gland (9 to 40.8 ppm). Schwimer (1973) determined levels of lead and fourteen other metal ions in the herbivorous gastropod *Olivella biplicata*, the predatory gastropod *Polinices lewisii*, and the predatory sea star *Pisaster brevispinus* collected at three different sites in California including a sewage outfall. Lead levels were found to be greatest for *Olivella* (4.6 to 11.8 ppm) and in the soft parts of *Polinices* (2.6 to 7.4 ppm). *Pisaster* tended to concentrate lead in the rays with a high lead value of 26.6 to 35.2 ppm. *Polinices* shells accumulated the greatest amounts: anterior shell, 10 to 22.4 ppm; shell spire, 21.7 to 39.1 ppm; and anterior shell, 18.1 to 34.5 ppm; shell spire, 21.7 to 39.1 ppm; and anterior shell, 18.1 to 34.5 ppm. *Olivella* shells accumulated 15.9 to 25.5 ppm. In the *Mytilus edulis* the largest amount of lead is accumulated in the kidney. (Schulp-Baldes, 1974).

Graham (1972) analyzed 6 species of mollusks from 11 locations in California for lead, silver, cadmium, chromium, copper, manganese, and zinc. The species examined included 2 herbivorous gastropods (*Acmaea digitalis* and *Tegula funebralis*), one predatory snail (*Thais emarginata*), 2 bivalves living on hard substra (*Mytilus Californianus* and *Medulis*), and 2 burrowing clams (*protothaca staminla*, and *Tapes semidecussata*). These species live in the intertidal zone, and near cities where they are exposed to atmospheric lead fallout from automobile exhaust. *M. Californianus* was also found in the vicinity of a sewer outfall. The lead content of the shells of these mollusks averaged less than 9 ppm lead on a dry-weight basis. Body-lead levels were as follows: *Acmaea digitalis* 931 ppm; *M. Californianus* 23.4 ppm; *Tegula funebralis* 9.8 ppm; *M. edulis* 7.9 ppm; *Protothaca staminea* 5.2 ppm; and *Tapes semidecussata*, less than 2.2 ppm.

In Mobile, Alabama, where the mean water-lead levels ranged from 0.5 to 3.0 micrograms per liter (ppb) Kopfler and Mayer (1973) found in oysters an average of 0.67 to 0.88 milligram lead per kilogram (ppm) wet weight. This concentration is about two times that of the average value for Atlantic Coast oysters. Pringle, et al., (1968) studied the uptake and concentration rates of approximately ten trace metals including lead in the Northern quahaug or hard-shell clam (*Mercenaria mercenaria*), the soft shell clam (*Mya arenaria*), the American (Eastern) and Pacific oysters (*Crassostrea virginia* and *C. gigas*) in their natural environment. Anatomical uptake of lead as well as depletion studies were conducted using the Eastern oyster. There were species differences in the uptake and concentration of lead. Temperature, salinity, dissolved oxygen, pumping rates, and the physiological conditions of the animal are all closely related to uptake and the concentration level. Clams (*Mya* and *Mercenaria*) and oyster (*Crassostrea*) collected along the Atlantic and Pacific coasts contained the following lead concentrations in parts per million (ppm) of wet weight: Eastern oyster, 0.10 to 2.30; Pacific oyster, 0.10 to 4.50; soft-shell clam, 0.10 to 10.20; and hard-shell clam or Northern quahaug, 0.10 to 7.50. Along the Atlantic coast the Eastern oyster, soft-shell clam, and Northern quahaug had average lead concentrations of 0.47, 0.70, and 0.52 ppm, respectively. The Pacific oyster had an average lead concentration of less than 0.20

ppm at various times of the year. Trace metal depletion studies carried out for 21 days showed that the Eastern oyster loses lead at the rate of 0.48 to 0.91 milligram per kilogram per day. There appeared to be a direct relationship between the uptake rate and its depletion for any molluscan species. The results of studies on the uptake and concentration of lead in the Eastern oyster, Northern quahaug, and soft-shell clam subjected to a simulated natural environment are summarized in Table 5.1. Under the same experimental conditions with the oyster and soft-shell clams, doubling the level of lead will result in twice the rate of uptake and tissue concentration reached in the same time period. The four environmental lead levels (0.025, 0.05, 0.1, and 0.2 ppm) gave identical results as to the concentration order in the anatomical storage studies. Anatomical areas in the order of their increasing lead concentration (ppm) were: muscle, 9 to 115; mantle edge, 15 to 192; mantle, 14 to 212; remaining body parts, 18 to 237; gill, 23 to 274, gonad, 26 to 235; and digestive gland, 28 to 368. The high lead concentrations in the liver (digestive gland) and gill indicate that these organs serve as areas for lead storage in the oyster. This correlates with the presence of large number of chelating organic ligands in these tissues.

Valiela, et al., (1974) found that the growth of Mercenaria mercenaria and Crassostrea virginica, bivalves found in tidal creeks in salt marshes along the East Coast, was not affected by the addition of sewage sludge containing 0 to 81.3 mg Pb/m^2 and urea fertilizers to salt-marsh plots. Growth of Modilolus demissus, a mussel inhabiting the marsh surface was enhanced in all fertilized treatments. However, no increases in lead content were obtained in any of the three species.

5.2.1.2 Effects--

Several studies have been conducted on the toxicity of lead to freshwater and marine protozoans. Apostol (1973) found that lead acetate at 500 milligrams per liter killed Paramecium caudatum; concentrations at 100 milligrams per liter only inhibited growth of this species. Carter and Cameron (1973) reported that lead nitrate was much more toxic to the ciliated protozoan Tetrahymena pyriformis in soft water than in hard water: 96-hr LT$_{50}$ was 42 ppm for soft water, and greater than 250 ppm for hard water. Growth of cultured Cristigera, a bacterivorous marine ciliate, was reduced 8.5 percent at a lead nitrate level of 0.15 ppm (Gray and Ventilla, 1973). Table 5.2 from Ruthven and Cairns (1973) illustrates the response of several free-swimming protozoans to lead as lead nitrate.

Karbe (1973) exposed the colonial hydroid Eirene viridula to varying concentrations of lead nitrate in natural seawater to assess the response of the polyps to pollutants. One to ten parts per million lead induced morphological changes and tissue reorganization of hydranths. The threshold lead concentration giving acute effects was 1 to 3 ppm. Siegel, et al., (1973) on exposure of planaria and Oniscus (Isopoda) to tetraethyllead recorded 50 percent survival times of 576 and greater than 1,000 minutes, respectively. Brown and Ahsanullah (1971) studied the toxicity of six metal salts including lead nitrate to Artemia salina (brine shrimp) and Ophryotrocha labronica (polychaete), and the effect of three selected

Table 5.1 LEAD ACCUMULATION IN A SIMULATED NATURAL ENVIRONMENTAL SYSTEM AT 20 C[a]

Shellfish Species	Environmental Lead Level, ppm	Total Accumulation, mg/kg	Accumulation Time, days	Accumulation Rate, mg/kg/day
Soft-shell clam	0.1	112	70	1.60
Soft-shell clam	0.2	235	40	5.80
Soft-shell clam	0.2	260	84	3.10
Northern quahaug	0.2	35	56	0.63
Eastern oyster	0.025	17	49	0.35
Eastern oyster	0.05	35	49	0.71
Eastern oyster	0.1	75	49	1.50
Eastern oyster	0.2	200	49	4.00

[a] Modified from Pringle et al.,(1968).

Table 5.2 CONCENTRATIONS OF LEAD NITRATE LETHAL TO OR TOLERATED BY SIX FREE-SWIMMING PROTOZOAN SPECIES[a]

	Concentration, ppm	
Species	Lethal[b]	Tolerated[c]
Chilomonas	320	5.6
Peranema	-	1000
Tetrahymena	>100	24
Paramecium multimicronucleatum	56	24
Euglena gracilis	-	1000
Blepharisma	100	42

[a] Source: Ruthven and Cairns. Reprinted with permission from Journal of Protozoology (c) Journal of Protozoology (1973).

[b] Lethal concentration - lowest concentration at which all organisms die in 10 minutes.

[c] Tolerated concentration - highest concentration at which some organisms were living after 3 hours.

metal salts on their growth rates. Lead was among the metals with low toxicity. Lead at 10 ppm was least toxic of the six metals to *Artemia* and *Ophryotrocha*, with LC_{50} being more than 600 and 576 hours, respectively, for *Ophyrotrocha* and *Artemia* adults. Exposure to a lead concentration of 10 ppm did not significantly suppress the growth of *Ophryotrocha* whereas exposure to 5 and 10 ppm lead significantly suppressed the growth rate of *Artemia*.

The toxicities of lead (as lead chloride) and other metals in Lake Superior water to *Daphnia magna* were evaluated on the basis of a 48-hr LC_{50}, a 3-week LC_{50}, and a 3-week 16 and 50 percent reproductive impairment (decrease in the number of young born). The acute 48-hr LC_{50} was 450 micrograms per liter when the daphnids had been fed. The lead concentrations giving a 3-week LC_{50}, and 50 and 16 percent reproductive impairments were 300, 100, and 30 ppb, respectively. Reproductive impairment was found to be a more sensitive measure of toxicity than survival. Lead was found to stimulate glutamic oxalacetic transaminase activity and to cause a decrease in weight, but there was little change in the protein content (Biesinger and Christensen, 1972). McKee and Wolf (1963) in their review of toxicity data point out that 0.01 to 1 ppm lead chloride in various kinds of water was deleterious to *Daphnia magna* after 10 days' exposure. In Lake Erie water 128 ppm lead chloride was found to be lethal to *Cyclops vernalis*. Wilder (1952) reported that lobsters died within 20 days when kept in lead-lined tanks but survived 60 days or longer in steel-lined tanks.

Whitley (1968) exposed two turbificid worms, *L. hoffmeisteri* and *T. tubifex* to 1 milligram of lead (as lead nitrate) per liter of modified Knop's solution. The 72-hr TLm (median tolerance limit) was 27.5 ppm at pH 8.5 and 49 ppm at pH 6.5. Warnick and Bell (1969) conducted static bioassays to determine the toxicity of some heavy metals to aquatic insects. With a high test concentration of 64 ppm, 96-hour TLm values were not found. Fifty percent survival times (LC_{50}) were as follows: *Acroneuria*, greater than 14 days at 64 ppm, *Ephemerella*, 7 days at 16 ppm, and *Hydropsyche*, 7 days at 32 ppm.

Pringle, et al., (1968) exposed American (Eastern and Pacific) oysters to four environmental lead concentrations (0.025, 0.05, 0.1, and 0.2 ppm). At lead concentrations of 0.025 and 0.05 ppm, the oysters appeared to be in good gross physiological condition. However, at 0.1 and 0.2 ppm, considerable toxicity was noted and the following anatomical changes occurred: (1) atrophy and diffusion of gonadal tissue; (2) less identifiable and lighter-colored hepatopancreas, (3) considerable edema, and (4) disappearing or less distinct mantle edge.

Calabrese, et al., (1973) studied the effect of eleven inorganic metallic salts on the survival of American or Eastern oyster embryos. The 48-hour LC_0 and LC_{50} for lead nitrate were 0.5 and 2.45 ppm, respectively. Lead concentrations greater than 6 ppm were necessary for 100 percent mortality. Calabrese and Nelson (1974) found that lead nitrate was lethal to hard-shell clam embryos at 1.2 ppm. LC_0, LC_{50}, and LC_{50} ranges for hard-shell clam embryos were 0.40, 0.78, and 0.72 ppm, respectively, in synthetic seawater.

Cleland (1953) found that approximately 200 ppm lead as lead nitrate in seawater produced abnormalities in the eggs of sea urchins. A concentration of only 124 ppm lead was required to suppress membrane elevation. At this concentration subsequent cleavage was mostly normal and polyspermic.

5.2.2 Terrestrial

5.2.2.1 Metabolism: Uptake, Absorption, and Residues--

Price, et al., (1974) sampled insect communities at sites for the level of lead emissions from motor vehicle exhausts. They found no significant differences in the lead content of insects among sample sites within the same traffic density and vegetation category, or among samples taken at different times of the year. However, in areas of high lead emission insects had average lead levels (ppm, oven dry weight) of 10.3, 15.5, and 25 for species that suck plant juices, chew plant parts, and prey on other insects, respectively. This does indicate a biomagnification of lead from herbivore to carnivore trophic levels. In low-lead emission areas insects in the same feeding categories had average lead contents of 4.7, 3.4, and 3.3 ppm. Giles, et al., (1973) determined the lead content of Japanese beetles (*Papillia japonica*), damselflies (*Agrion maculatum*), and the European mantid (*Mantis religiosa*) collected along Baltimore, Maryland's major north-south freeway (I-83), which in 1970 had an average daily traffic count of 13,000 vehicles, and in a control area 480 meters west of the freeway. Japanese beetles had 7.1 and 9.0 ppm lead, respectively, in control and freeway areas. Their host plants (wild carrot and evening primrose) contained 3.0 and 4.3 ppm, respectively, in the control area and 9.4 and 15.7 ppm in the freeway area. Since these insects are strong fliers, there is a possibility of intermingling of individuals from the control and freeway areas. This species spends only a few months of its life cycle above ground thereby limiting the time lead can be accumulated from feeding on contaminated plant parts. The damselfly is a weak flier so the imagoes were probably indicative of environmental conditions of the collection sites. In the control area lead levels in damselfly imagoes ranged from 6.83 to 6.97 ppm; in the freeway area, 7.08 to 9.09 ppm. European mantid nymphs and imagoes in the control area had respective lead levels of 2.04 ppm, and 1.27 and 1.94 ppm. In the freeway area 7.35 ppm (nymphs), and 3.52 and 14.80 ppm (imagoes) lead were present. It did appear that measurable amounts of atmospheric lead were being concentrated by these insect predators.

Nehring (1976) studied the acute toxicity of some heavy metals to a mayfly (*Ephemerella grandis*) and a stonefly (Pteronarcys californica). Flow through methods were used, with a dilution water whose alkalinity and hardness varied from 30 to 70 ppm (as Ca CO_3) between tests, but not more than 10 ppm within a test. The 14-day LC_{50} values were greater than 19.2 ppm lead for the stonefly, and 3.5 ppm lead for the mayfly.

Gish and Christensen (1973) found that lead, cadmium, nickel, and zinc in soils and earthworms decreased with increasing distances--3, 6, 12, 24, and 48 meters (10, 20, 40, 80, and 160 feet) from the Baltimore-Washington Parkway and U.S. Highway No. 1. Highest lead concentrations in soils and in earthworms along either highway were found in plots closest to the roadway. Lead concentrations in soils and earthworms along the

Parkway with a traffic density of 47,800 and 44,500 cars per day were 228 and 93 ppm, and 121 and 107 ppm, respectively. Along U.S. No. 1 with a traffic density of 25,100 and 25,600 cars per day, soils had 63.7 and 83.5 ppm lead and earthworms had 64 and 76.7 ppm lead. The maximum lead level accumulated by earthworms was 331 ppm which might be lethal to animals that feed on earthworms. The mean lead concentrations for the two highways combined at distances of 3 to 48 meters (10 to 160 feet) from the roadway were 468 to 53.4 ppm (soils) and 270 to 52.7 ppm (earthworms). Lead levels in earthworms averaged 0.95 times those in the soils. The ratios of lead in earthworms to those in soil tended to increase as distance increased. Lead levels at 3 meters (10 feet) from the roadway, though higher at other distances, were half those in the soil. At other distances, the levels were approximately equal. Differential accumulation by earthworms (Alabophera, Lumbricus, and Octolasium) of cadmium, lead, and zinc in six soil series in east Tennessee was determined by Van Hook (1974). Mean lead concentrations in soils and earthworms were 27 and 4.7 ppm, respectively. The mean earthworm concentration factor for lead was 0.2, ranging from 0.1 in Emory soil to 0.3 in Captina soil. Lead was not biologically accumulated by earthworm species studied. Based on the results obtained, Van Hook believes that earthworms could serve as useful biological indicators of increased lead, cadmium, and zinc contamination of soils because of the fairly consistent relationship between element concentrations in earthworms and soils. These invertebrates are key components in natural food chains and are a food source for many small mammals and birds.

5.2.2.2 Effects--

Lower (1975) used the vinegar fly, Drosophila melanogaster, to monitor the environmental enrichment of lead, cadmium, cpper and zinc at geographically separated lead smelting facilities in Missouri. Changes in gene frequency in five of ten isozyme loci in Drosophila were significantly correlated with distance from a smelter which has been operated since 1968 at Bixby, Missouri. Enrichment also occurred at other locations. At lead concentrations of 12 to 1,200 ppm, the frequencies of alleles decreased at the four loci which had been definitely correlated with lead and cadmium. The changes in frequencies occurred over a distance of 11 kilometers with the greatest change in the first 5 kilometers. Seasonal changes in gene frequencies did not mask those changes associated with distance from the Bixby smelter or metal concentrations. The author postulates that intensive selection pressure is the cause of the changes. This study further confirms that lead interferes with mitotic and other essential functions (see Sections 4.3.2.2 and 6.3.1.). Further investigations utilizing D. melanogaster might clarify the mode of action of lead and other heavy metals within animal cells.

5.3 FISH

5.3.1 Metabolism: Uptake, Absorption, and Residues

Naturally occurring levels of lead in fishes are subject to variations due to age and species, fluctuations and differences in water chemistry, and geographical location. A survey of 419 fishes from 49 New York State waters reported concentrations of lead (analyzed colorimetrically) ranging generally from 0.3 to 1.5 ppm; a few specimens contained as high as 3 ppm (Pakkala, et al., 1972). In this study no correlation was drawn between the lead concentrations found in fish and the proximity to large cities, industrial effluents, rural areas or known lead deposits. A study of trace metals in Cayuga Lake lake trout (Salvelinus namaycush), aged 1 to 12 years, showed lead levels (decapitated and eviscerated fish) between 4.4 ppb and 22 ppb (Tong, et al., 1974). While highest concentrations for lead occurred in fishes 1 and 2 years old, no significant ($P = 0.05$) correlation between age and concentration was drawn.

Holcome, et al., (1976) studied the long term effects of lead on three generations of brook trout. They found that the greatest accumulation of lead occurred in the kidney, liver, and gill tissue. Kidney and liver lead residues from second generation fish reached an equilibrium at various exposure concentrations, then tended to remain at that level or decrease with continuing exposure. The maximum mean residue levels for liver and kidney samples, respectively, were 68 and 215 ppm lead in tissue for first generation fish and 50 and 179 ppm lead in tissue for second generation fish exposed to 119 ppb lead. Lead residues in gill tissue did not reach an equilibrium based on ppm lead but tended to increase with continuing exposure. Muscle tissue did not accumulate lead to any substantial extent. The mean average lead residue values for all muscle tissue for test fish and controls were 2.1 and 1.1 ppm lead, respectively.

Lead has been found to accumulate at higher concentrations in certain fish tissues. In a study of fishes from a lake located near a lead mine in Sweden, concentrations of lead were 12 ppm in liver, 5.7 ppm in gills, and 1.4 ppm in muscle (Wetterberg, 1966). Stevens and Brown (1974) found less than 0.2 ppm of lead, dry weight, in muscle, liver, epigonal and gonad tissue of 98 percent of blue sharks studied; some individuals contained concentrations of lead as high as 1.8 ppm in epigonal plus gonad tissue. In a study of flounders, Hardisty, et al., (1974) found the highest lead concentrations to be in brain tissue (3.85 to 43.6 ppm). These authors also found that lead levels in muscle tissue rarely exceed 20 percent of the values for liver, heart, or kidney, which range from 20 to 30 ppm for flounders. The largest flounders (length and age class) exhibited the highest concentrations of lead; no consistent seasonal variation was apparent. Chow, et al., (1974), found that 3 percent of all lead in tuna resides at a concentration of 0.003 ppm in fresh muscle; 52 percent resides in epidermis at 2 ppm. Muscle comprises 75 percent of the total body weight; epidermis amounts to one quarter of 1 percent, yielding a total body burden of lead in albacore tuna of 0.008 ppm. (Interestingly, Chow, et al., (1974) state that contamination by industrial lead raises the concentrations of lead in tuna processed for human consumption about 1,000 times that found in living tuna. Concentrations in the mucosal slime could only raise muscle concentrations by a factor of 20 by contamination.) Table 5.3 presents lead values found in tissues of sardines and anchovies (Gilmartin and Revelante, 1975). Increased lead concentrations in skin tissue during the winter sampling were possibly due to resuspension of sediments by the wind.

Chow, et al., (1974) claim that values reported for lead in materials such as sea water and fish tissue may be erroneously high. They state

Table 5.3 CONCENTRATIONS OF LEAD IN TISSUES OF SARDINE AND ANCHOVY FROM THE ADRIATIC SEA[a]

	Lead Concentration, ppm, Wet Weight					
	Skin	Gills	Muscle[b]	Digest[b]	Liver[b]	Total Fish
Sardine:						
June 9, 1972	4.5	3.0	0.4	ND	ND	1.23
July 10, 1972	4.9	4.5	0.1	ND	ND	0.94
August 17, 1972	4.3	2.6	ND	ND	ND	0.82
September 29, 1972	5.3	1.9	ND	2.2	ND	0.84
October 31, 1972	3.3	2.4	ND	0.7	ND	1.38
December 5, 1972	6.8	3.1	ND	0.3	ND	1.40
Mean	4.9	2.9	0.1	0.5	ND	1.1
Anchovy:						
June 9, 1972	2.7	4.3	ND	ND	ND	0.99
July 10, 1972	5.2	3.7	ND	0.4	ND	0.99
August 17, 1972	5.7	3.9	ND	0.3	1.1	0.51
October 3, 1972	1.6	2.6	ND	1.3	1.5	0.73
October 31, 1972	7.0	3.1	1.2	0.7	3.4	1.16
December 6, 1972	6.5	3.9	0.3	0.4	11.0[c]	1.37
Mean	4.8	3.6	0.3	0.5	1.2	1.0

[a] Adapted from Gilmartin and Revelante (1975).

[b] ND = not detected.

[c] Suspect value - excluded from mean.

"not one oceanographic laboratory of superior status could, as of September, 1973, collect and analyze lead in coastal surface seawater by atomic absorption or anodic stripping voltammetry techniques and report reliable results." Based upon their findings of lead concentrations in tuna they state further "These new findings strongly suggest, as in the case of seawater, that recent studies of the hazards of lead pollution may be misleading if they are based on analyses of plant and animal tissues determined by routine analytical methods carried out without the use of clean-laboratory techniques and without the necessary sensitivity and accuracy." The method these workers employed was stable isotope dilution using thermal ionization source high-resolution mass spectrometers and special clean-laboratory techniques. They found that tuna muscle, uncontaminated by handling, contained approximately 0.0003 ppm lead (wet weight). However, commercial canned tuna muscle contained amounts of lead in the order of 0.1 to 0.9 ppm.

Much evidence exists for elevated amounts of lead in fishes because of environmental pollution. Fingerling brook trout previously exposed to increased invironmental lead concentrations due to snowmobile exhaust (4.1 ppb of lead before freezing and 135 ppb after ice-melt) were found to contain nine to sixteen times more lead than control fishes (Adams, 1974; Adams, 1975). Lead levels in muscle tissue of the wooly sculpin (*Clinocottus analis*) were found to increase from a rural tidepool area of California to an area receiving atmospheric lead pollution (Alley, et al., 1974). For this species, "control" levels were 0.6 ppm; fishes from polluted areas contained 2.7 ppm and 4.9 ppm. Pagenkopf and Neuman (1974) obtained similar results in a study of lead concentrations in fish tissue from a hatchery (1.41 ppb) and from the West Gallatin River in Montana (2.56 to 2.96 ppb). Mean concentrations of lead found in bone, liver, and gill tissue from the two sites were 0.95 and 3.85 ppm, 0.61 and 1.56 ppm and 0.62 and 2.43, respectively. Van Coillie and Rousseau (1974) found that the lead content in scales from fishes in waters of undetectable lead concentration was 2.89 times lower than in scales from fishes in water of 3.0 to 13.0 ppb lead. Mathis and Cummings (1973) reported on the lead in sediments, water, and biota of the Illinois River. A concentration gradient ranging from the highest level in worms, intermediate levels in clams, and lowest levels in fish fillets was found for lead. There was no statistical significant difference ($P = 0.05$) between the lead concentration of the muscle tissue of omnivorous and carnivorous fish.

Although there is evidence for methylation of lead by bottom s diment microorganisms, its implication for fish contamination is not presently known (Wong, et al., 1975).

5.3.2 Effects

Elevated lead concentrations have been proven to be toxic or deleterious to fishes. Table 5.4 presents a compilation of lead concentrations which were found lethal or toxic to fish under the conditions specified. Table 5.5 presents a similar compilation for lead compounds.

Table 5.4 CONCENTRATIONS OF LEAD REPORTED TOXIC OR LETHAL TO FISH[a]

Concentration of Lead, ppm	Type of Water	Time of Exposure	Species of Fish
0.1	--	--	Fish
0.1	--	--	Sticklebacks
0.1-0.2	Very soft	--	Sticklebacks
0.2	Soft	--	Fish
0.21	--	--	Guppy
0.25	Fresh	--	Fish
0.33	--	--	Minnows, brown trout and sticklebacks
0.34	1000-3000 mg/l of dissolved solids	48-hr TLm	Sticklebacks and coho salmon
1.0	--	Long term	Carp
1.0	--	8.5 days	Sticklebacks
1.4	Soft	18-24 hr	Rainbow trout
1.4	Tap	48-hr TLm	Bluegill sunfish
2.8	Fresh	--	Fish
4.0	Soft	10-12 hr	Rainbow trout
5.5	Stream water	--	Trout
6.3	Tap	24 & 28 hr TLm	Bluegill sunfish
10.0	--	--	Goldfish
17.0	--	--	Goldfish
27.0	Tap	16-183 days	Catfish
40.0	--	80-hr	Goldfish
63.0	--	80-hr	Goldfish

[a] Adapted from McKee and Wolf (1963).

Table 5.5 CONCENTRATIONS OF LEAD COMPOUNDS REPORTED LETHAL TO FISH[a]

Lead Compound	Concentration, ppm	Type of Water	Time of Exposure	Type of Fish
Lead acetate	5.	--	4-16 hr	Minnows
	10.	--	12 days; renewed every 2 days	Goldfish
	10.	Stream		Trout
Lead arsenate	25.	--	24-hr	Trout
Lead chloride	0.33	Fresh		Fish
	0.58	Lake Erie		White fish fry
Lead nitrate	0.16	Tap	--	Stickleback
	0.53	Tap	--	Minnows, sticklebacks, and brown trout
	3.	--	12-hr	Topminnows
	5.	--	2-hr; 1.4 mg/1 dissolved oxygen	Goldfish
	10.	Natural	2.5-hr	Trout
	10.	Tap	24 and 48-hr TLm	Bluegill sunfish
	10.	Hard	4 Days	Goldfish
	16.	--	--	Goldfish
	16.	--	20-hr	Minnows
	100.	Hard	80-hr	Goldfish
	165.	Distilled	--	Fish
	240.	Highly turbid	96-hr TLm	Mosquitofish
	830.	--	3-hr	Minnows
	3320.	--	2.2-hr	Minnows
	8300.	--	1.5-hr	Minnows
	16600.	--	1.4-hr	Minnows
	44000.	--	44 min	Minnows
	53000.	--	40 min	Minnows

[a] Adapted from McKee and Wolf (1963).

It is commonly theorized (McKee and Wolfe, 1963; Pakkala, et al., 1972) that in waters containing lead salts, a film of coagulated mucus forms, first over the gills, then over the whole body of the fish (possibly the result of a reaction of lead with an inorganic constituent or mucus), Death is then by suffocation. A report by Aronson (1971) states that recovery does occur when this mucosal film is shed and that analysis of the film accounts for virtually all the lead in solution.

Certain species of fishes are more susceptible to lead than others. The action of lead on goldfish is the same as for trout, sticklebacks, and minnows, yet goldfish are more resistant. Goldfish appear to tolerate 1 ppm lead in soft tap water (Jones, 1938). In soft tap water 0.1 to 0.2 ppm lead proved fatal to sticklebacks (McKee and Wolf, 1963). Variations in tolerance may be related to the nature of the gill secretions; goldfish produce copious amounts (Aronson, 1971b).

More subtle effects have been shown to occur at chronic exposures to lead. An early study by Dawson (1953) of 16- to 183-day exposures of catfish (Ameriurus nebulosus, genus name since changed to Noturus) to 5 ppm lead acetate renewed every 48 hours yielded early evidence of blood cell injury and elicited a mild regenerative response. After several weeks exposure, Dawson reported the occurrence of injured erythrocytes, progressive anemia, and marked regenerative response in peripheral blood. During lead poisoning the erythropoietic activity of the spleen was greatly reduced and the organ itself became smaller and paler. In fishes killed by lead poisoning, Dawson reported an extreme dilation of the gall bladder. The prolonged exposures of this study gave evidence of lead absorption. Similar physiological effects have been noted in guppies at long-term exposures.

Lead has been found to interfere with enzyme activities (see also Section 6.3.1). Jackim, et al., (1970) found lead to inhibit alkaline phosphatase activity in in vitro studies on killifish (Fundulus heteroclitus), but increased activity of the same enzyme in in vivo studies, both at 96-hour TLm concentrations (i.e., 188.0 ppm).

Experiments on various life stages of fishes indicate that susceptibility to lead is greatest during embryo and fingerling stages. Highest mortality rates in life stages of brook trout (Salvelinus fontinalis) occur among alevins upon exposure to lead nitrate (Christensen, 1975). Alkaline phosphatase and acetylcholine esterase activity were increased at 525 ppb of lead in tissue or water. A decrease in weight in response to 134 ppb and 525 ppb of lead was also noted.

McIntyre (1972) reports severe embryo deformation in the eggs of brook trout at 500 ppb of lead. Similar deformation as well as increased incidence of blacktail syndrome occurs in fathead minnows at 240 ppb. Lead concentrations of 25 ppm administered daily as a single dose under diurnal fluctuations of temperature and disolved oxygen conditions reduced growth of fingerling brook trout (Dorfman and Whitworth, 1969).

Of the factors possibly influencing the toxicity of lead to fishes such as dissolved oxygen concentration, pH of solution, volume and number of exchanges of experimental solution, and duration of exposure, water temperature and, particularly, water hardness appear to be important controlling factors. A 10-degree C rise in temperature has been shown to reduce survival time by 50 percent (Aronson, 1971). An increase in water hardness from 14 to 53 milligrams per liter (expressed as calcium carbonate) decreased lead concentration from 8 to 1.6 ppm by precipitation. Fifty ppm of calcium destroyed the toxic effect of 1 ppm of lead (McKee and Wolf, 1963). Calcium has been shown to antagonize toxic lead effects by increasing survival times of fishes exposed to 1 ppm of lead nitrate with an increase of calcium nitrate or chloride concentration. In this case, lead toxicity is not reduced by precipitation, but by prevention of the coagulation of mucus (Jones, 1938).

In an extensive study of chronic lead exposure to rainbow trout, Davies and Everhart (1973) determined toxic levels for lead nitrate in hard and soft waters. Since lead may form complexes or precipitate in hard water, the concentration of the metal was expressed on a total and dissolved lead basis. On a total lead concentration basis, the 96-hr TL_{50} (50 percent tolerance limit) was 471 ppm and the MATC (maximum acceptable toxicant concentration) was 0.12 to 0.36 ppm. The MATC was determined by the occurrence of abnormal black tails. On a dissolved lead basis, the 96 hr TL_{50} was 1.38 ppm and the MATC 0.018 to 0.32 ppm. Lead was considered to be completely dissolved in soft water. The 18-day TL_{50} in soft water was 140 ppb and the MATC was between 6 to 11.9 ppb. The authors developed an application factor approach that may be utilized to compare the toxicity of lead in different water qualities where the soluble or free lead in water is determined.

This same study by Davies and Everhardt (1973) investigated the occurrence of physical abnormalities in the F_1 generation of brook-stock rainbow trout that were used in the soft water bioassay. Again, no growth or hematological differences were apparent after 6 months' exposure to lead concentrations ranging from 3.1 to 95.6 ppb. Black tails, spinal curvatures and/or eroded caudal fins occurred at concentrations of 11.9 ppb and greater. No effects were noted at lower concentrations. From this entire study, the maximum acceptable lead level for rainbow trout is very near 11.9 ppb.

From this survey it can be concluded that the effects of lead on fishes may be so severe as to cause direct mortality or be so subtle as to be manifested only after an exposure of considerable duration. Body surfaces, internal organs or metabolic activities may be affected. Detrimental effects include not only mortality but also abnormal behavior rendering the fish more vulnerable to predation. Interference with metabolic activity, while not only eliciting abnormal behavior, may subject the fish to attack by disease or parasites. Reproductive success may also be limited due to the high susceptibility of embryos and fingerlings to lead effects.

Lead concentrations in water are subject to complex chemical interactions. Toxicities may be enhanced or reduced by fluctuation in temperature, dissolved oxygen or concentrations of minerals. There is need for further investigation to determine maximum acceptable levels under various water chemistry conditions.

5.4 BIRDS

Concentration of lead in tissues of birds and physiological effects of lead on birds have mainly been studied in waterfowl, particularly with respect to the ingestion of lead shot (Anderson, 1975; Bellrose, 1959; Coburn, et al., 1951; Karstad, 1971; Longcore, et al., 1974a; Longcore, et al., 1974b). The mallard (*Anas platyrhynchos*) is the duck most frequently associated with lead poisoning dieoffs. Use of shotguns in marshes and lakes by hunters concentrates lead shot on the bottom of heavily hunted areas. The spent shot is eaten by waterfowl as if it were seeds or grit. As the shot are held in the duck's gizzard, the lead is absorbed into the body, causing an estimated 2 to 3 percent of the American waterfowl population to die annually from lead poisoning (Stickel, 1969). Mortalities due to lead ingestion by Canadian and United States waterfowl (mostly mallards, mottled ducks, redheads, and black ducks) have been estimated to be 1.6 to 2.4 million annually out of fall flight population of 100 million ducks. This great loss has prompted the preparation of an environmental impact statement on the use of steel shot for hunting waterfowl (U.S. Department of the Interior, 1976).

Although waterfowl (includes ducks, geese, and swans) has been the major bird group studied for lead poisoning, other bird groups have also been analyzed for lead concentration in various tissues and/or examined for the presence of lead shot. Studies of lead in nonwaterfowl game species include species-specific studies of the sora rail (*Porzana carolina*) (Artmann and Martin, 1975) and ring-necked pheasant (*Phasianus colchicus*) (Lynch, 1973: Anderson and Stewart, 1969), and a general survey of 28 bird species, including grouse, ptarmigan, rails, doves, and ring-necked pheasants (Bagley and Locke, 1967). USDI (1976) lists cases of lead poisoning in godwits, California gulls, and several species of the order Gruiformes (rails, gallinules, and coots).

Investigations of lead in nongame bird species are not nearly as numerous as studies involving game birds. Bagley and Locke (1967) reported on lead concentrations in six nongame bird species. Snyder, et al., (1973) reported on lead levels in eggs of Cooper's hawks (*Accipiter cooperii*). Two reports on starlings (*Sturnus vulgaris*) discussed lead levels at monitoring sites throughout the United States (Martin and Nickerson, 1973; Martin, 1972). Lincer and McDuffie (1974) reported on lead levels in American kestrel (*Falco sparverius*) eggs. Lead poisoning in a prairie falcon (*Falco mexicanus*) was described by Benson, et al., (1974). Finally, two studies analyzing lead levels in herons (Hoffman and Curnow, 1973) and common terns (*Sterna hirundo*) (Connors, et al., 1975) found that lead concentrations in most specimens were below the detection limits of the analytical procedure used.

5.4.1 Metabolism: Uptake, Absorption, and Residues

Extensive studies of naturally-occurring lead levels in single species include analysis of starlings (Martin, 1972; Martin and Nickerson, 1973), pigeons (Tansy and Roth, 1970), and ring-necked pheasants (Anderson and Stewart, 1969). Whole body, wet-weight lead residues of starlings sampled throughout the United States varied from 0.4 ppm at Yakima, Washington, to a high of 13.3 ppm at Chicago, Illinois, with a mean level of 3.18 ppm for all sample sites (Martin, 1972). Lead residue levels were highest in birds from urban areas, reflecting the greater exposure of starlings to automotive and industrial contamination. The mean lead content per unit weight of hard (feathers, nails, beak, femur) and soft tissues (liver, kidney) of randomly procured Philadelphia City pigeons was significantly higher than the corresponding values for country pigeons (see Figure 5.1). Interestingly, blood-lead levels of the city birds were as low as, if not lower than, their country counterparts (Tansy and Roth, 1970).

Lead concentrations in the liver are considered to be the most useful of all tissue types in diagnosing lead poisoning (Longcore, et al., 1974a) and high levels are indicative of severe, recent exposure. Therefore, most studies have included liver analysis in their sampling plan. One of the best summaries of lead concentrations in livers of lead-poisoned waterfowl (Table 5.6) indicates that lead levels of 6 to 20 ppm in the liver of waterfowl are diagnostic of active lead intoxication (Longcore, et al., 1974a). On the other hand, background levels of lead in eleven species of waterfowl with no known history of lead exposure averaged 0.5 to 1.5 ppm (Bagley and Locke, 1967; see Table 5.7).

One of the most complete studies of naturally-occurring lead levels in liver tissues of a variety of birds was done by Bagley and Locke (1967) on 28 species of wild birds. They found that the average background lead concentrations in the livers of these birds varied from 0.5 to 3.7 between species (see Table 5.7). Lead levels in livers of ringnecked pheasants from Illinois varied from 0.09 to 0.84 ppm (Anderson and Stewart, 1969). Lynch (1973 found a geometric median concentration of 1.59 ppm (see Table 5.8) in the livers of ring-necked pheasants.

Lead residues in bones are normally higher than those in liver, but seem to be less diagnostic of lead poisoning (Stickel, 1969). Lead accumulates in bone from both acute, high-level exposure or chronic, low-level exposure. Therefore, high bone lead levels are not suitable for diagnosing lead poisoning, but do indicate chronic exposure to lead.

Lead is stored in the bones of waterfowl and may be present in varying amounts depending on several factors, including diet, and duration and levels of exposure. High levels of lead (67 to 73.6 ppm) were found to occur in wing bones of mallards, for example, as a result of ingestion of a single lead shot. Food in the form of commercially prepared duck ration reduced the amount of lead (2.3 ppm) absorbed and deposited in the bones (USDI, 1976). Longcore, et al. (1974a) found a geometric mean lead concentration in the tibia of lead-dosed mallards that died to be 137 ppm.

Lead levels in femurs of eleven Ohio ring-necked pheasants had a median of 8.0 ppm and a range of 1.8 to 17.1 ppm, wet weight (Lynch, 1973; see Table 5.8). The average background lead concentration in tibias of 12 species of wild birds varied from 2.0 ppm in eleven Canada geese (Branta canadensis) to 13 ppm in 18 snow geese (Chen hyperborea) (Bagley and Locke, 1967).

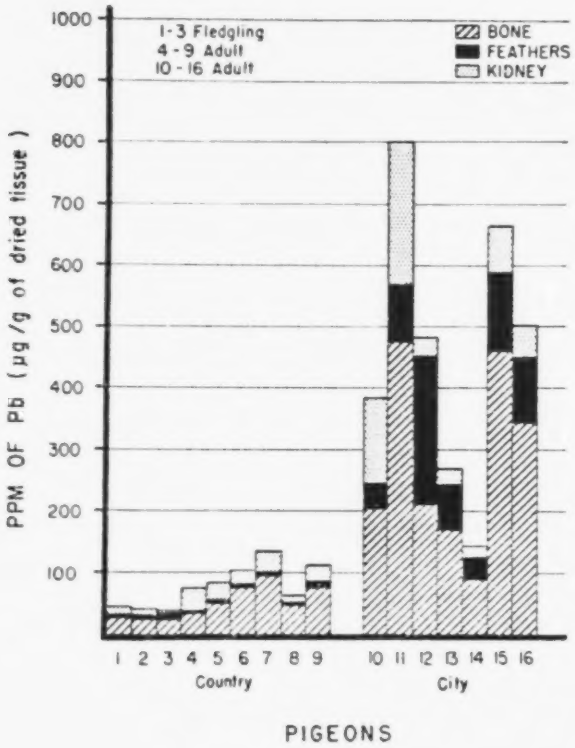

Figure 5.1 Tissue lead concentration of country and city pigeons. Source: Tansy and Roth. Reprinted with permission from Journal of Air Pollution Control Association.
(c) Air Pollution Control Association, 1970.

Table 5.6 LEAD CONCENTRATIONS IN LIVERS OF LEAD POISONED WATERFOWL[a]

Species	Source	Amount Lead (ppm, wet wt.)[b]		References
		Average	Range	
Canada geese	"die-off"	18	9-27	Adler (1944)
Canada geese (2 separate die-offs)	"die-off"	12 22	1-20 12-53	Bagley et al., (1967)
Canada geese	expt'l.	20	5-32	Cook & Trainer (1966)
Canada geese	expt'l.	19	8-42	Karstad (1971)
Canada geese	"die-off"	26	12-44	Locke et al. (1967)
Canada geese	"die-off"	21	10-45	Locke & Bagley (1967a)
Mallards	expt'l.	33	20-64	Bates et al. (1968)
Mallards	expt'l.	44	23-80	Coburn et al., (1951)
Mallards (2 separate groups)	expt'l.	12 40	8-14 11-16	Barrett & Karstad (1971)
Mallards	expt'l.	51	16-76	Locke et al., (1966)
Whistling swan	"die-off"	28	18-37	Chupp & Dalke (1964)
Mallard		12	12	
Mute swan	"die-off"	--	1-70	Erne & Borg (1969)
Mallard		--	5-45[c]	
Mallard	expt'l.			Andrews et al., (unpublished data, Patuxent Wildlife Research Center)
	(died: corn diet)	29	8-66	
	(died: comm. mix pellet diet)	23	19-26	
	(survived: comm. mix pellet diet)	1	1-3	
Black duck	"die-off"	25	25	Locke & Bagley (1967b)

[a] Adapted from Longcore et al. (1974a).
[b] Values rounded to nearest whole number.
[c] This range of values for more than half of the livers examined.

Table 5.7 THE CONCENTRATION OF LEAD IN THE LIVER OF BIRDS[a]

	Average, ppm[b]	Range, ppm[b]	No. of Samples	Source[c]
American coot (*Fulica americana*)	2.0	2.0	1	3
American scoter (*Oedemia nigra americana*)	0.5	0.3-0.9	10	2
Bald Eagle (*Haliaeetus leucocephalus*)	0.6	0.6	1	2
Black duck (*Anas rubripes*)	0.5	0.4-0.6	2	2
Brant (*Branta bernicla*)	1.3	0.9-1.9	11	2
Brown pelican (*Pelecanus occidentalis*)	0.8	0.4-1.3	16	2
Canada goose (*Branta canadensis*)	0.5	0.3-0.8	11	1
Canvasback (*Aythya valisineria*)	0.5	0.5	4	2
Cowbird (*Molothrus ater*)	3.7	2.0-5.0	4	2
Domestic goose (*Anser cygnoides*)	0.6	0.3-0.8	4	1
Dusky grouse (*Dendragapus obscurus*)	1.1	1.1	1	1
Great blue heron (*Ardea herodias*)	0.7	0.7	1	2
Green wing teal (*Anas carolinensis*)	1.5	1.5-1.6	2	3
Hooded merganser (*Lophodytes cucullatus*)	0.9	0.6-1.2	3	2

Table 5.7 THE CONCENTRATION OF LEAD IN THE LIVER OF BIRDS[a]
(Continued)

	Average, ppm[b]	Range, ppm	No. of Samples	Source[c]
King rail (*Rallus elegans*)	2.0	2.0	1	2
Mallard (*Anas platyrhynchos*)	0.9	0.3-2.0	16	1
Mourning dove (*Zenaidura macroura*)	3.3	0.4-7.0	27	2
Osprey (*Pandion haliaetus*)	1.5	1.5	1	2
Pintail (*Anas acuta*)	0.9	0.9	1	3
Ring-necked pheasant (*Phasianus colchicus*)	0.5	0.2-1.0	21	1
Rock ptarmigan (*Lagopus mutus*)	2.1	2.0-3.0	7	3
Sandhill crane (*Grus canadensis*)	0.7	0.7	1	2
Shoveler (*Spatula clypeata*)	1.1	1.0-1.2	3	3
Snow goose (*Chen hyperborea*)	1.2	0.8-1.8	18	2
Surf scoter (*Melanitta perspecillata*)	0.9	0.4-2.0	23	2
Whistling swan (*Olor columbianus*)	0.8	0.8	1	2
White-winged scoter (*Melanitta fusca*)	0.8	0.3-1.8	18	2
Wood duck (*Aix sponsa*)	1.5	0.7-2.0	5	2

[a] Bagley and Locke. Reprinted with permission from Bulletin of Environmental Contamination and Toxicology. (c) Springer-Verlag New York, Inc., 1967.

[b] Wet weight basis.

[c] (1) = Pen raised; (2) = captured or shot; (3) = found dead.

Table 5.8 LEAD CONCENTRATIONS IN TISSUE SAMPLES FROM OHIO RING-NECKED PHEASANTS[a]

			Pb Concentration, ppm, Wet Weight		
Tissue	No. Analyzed	No. Positive[b]	$\overline{X}$±S.D.[c]	Median	Range
Brain	1	0	n.d.[d]	n.d.	n.d.
Breast muscle	33	8	1.61±0.66	n.d.	n.d.-2.59
Feather	18	9	6.70±5.22	0.66	n.d.-19.66
Femur	11	11	8.83±4.53	7.98	1.76-17.12
Kidney	2	0	n.d.	n.d.	n.d.
Leg muscle	14	2	0.99±0.79	n.d.	n.d.-1.60
Liver	11	9	1.75±0.43	1.59	n.d.-2.41
Ovary	1	0	n.d.	n.d.	n.d.

[a] Source: Lynch, from M.S. Thesis, The Ohio State University (1973). Reprinted with permission of the author.

[b] Number of tissue samples with detectable lead concentrations.

[c] Mean±one standard deviation of tissue samples with detectable lead concentrations.

[d] n.d.-no lead detected. Below detection limit of 0.03 ppm lead.

Lead concentrations in brain tissues appear to have some value in diagnosing lethal lead toxicosis (Longcore, et al., 1974a). Lead levels in mallard brain tissue of more than 3 ppm indicate acute exposure to lead. Lead levels in brains of lead-dosed ducks that died of lead poisoning averaged 4.6 ppm and ranged from 2.1 to 10.6 ppm.

Lead concentrations in kidneys are also quite useful in diagnosing lead poisoning. High levels in the kidney are indicative of recent, high exposure to lead. Lead levels of 20 ppm in kidney tissue of mallards indicate acute exposure to lead. The average lead level in kidneys of lead-dosed mallards that died was 175.7 ppm (Longcore, et al., 1974a).

Lead concentrations of 10 ppm in clotted blood from mallard hearts are indicative of acute exposure to lead. In mallards dosed with lead shot, lead levels in blood from hearts averaged 10.2 ppm for ducks that died (Longcore, et al., 1974b). High concentrations of lead in red blood cells of lead-poisoned mallards also have been reported by Clemens, et al., (1975).

Many other bird tissues such as breast muscle, feathers, leg muscle, ovary, gall bladder, spleen, and lung have been analyzed for lead concentrations, but only lead levels in liver, brain, kidney, and blood appear to have value in indicating lead poisoning (Longcore, et al., 1974a; Lynch, 1973; see Table 5.8).

Presumably raptors feeding on ducks containing lead shot could accidently ingest lead shot. USDI (1976) indicates that there are only two published reports of secondary lead poisoning in birds (an Andean condor, *Vultur gryphus* and a prairie falcon, *Falco mexicanus*, both of which were in captivity). The prairie falcon was fed a diet of mallard duck heads, some of which contained at least one shot and/or lead residues of 2 to 55.8 ppm (muscle tissue) and 4.7 to 32.6 ppm (brain) (Benson, et al., 1974). The Andean condor had been fed hunter-killed cottontail rabbits, squirrels and groundhogs (Locke, et al., 1969).

5.4.2 Effects

The typical signs and lesions of lead poisoning in waterfowl are well described. Lead-poisoned waterfowl that are fairly well advanced in lead intoxication usually exhibit the following signs of poisoning:

1) varying degree of emaciation (loss of up to 40 percent of original body weight, and prominent keel portion of the sternum)
2) reduced activity with reluctance to fly
3) lowered food intake
4) palsy (wing droop)
5) bile staining of vent area
6) tendency to seek isolation and cover
7) loss of ability of walk or stand (USDI, 1976).

The internal lesions associated with lead-poisoning in waterfowl include:

1) lack of fat
2) atrophy of striated muscle, liver and kidneys
3) excess fluid in the pericardial sac
4) distended gall bladder
5) atrophied gizzard with grinding pads hardened and bile-stained
6) proventriculus impacted with food and grit
7) anemia and paleness of the whole body (USDI, 1976).

Lead poisoning typically causes a variety of lesions in ducks, such as emaciation, proventricular impaction, green-stained and eroded gizzard lining, atrophied liver, distended gall bladder, hydropericardium, and acid-fast intranuclear inclusions in kidney tubules. These abnormal changes were monitored in mallard drakes exposed to particulate lead in four concentrations (0, 17.8, 89.0, and 178 grams per square meter) in simulated marsh areas over a 14-week period. None of the above lesions was noted at necropsy in the control (no particulate lead) or low (17.8 grams per square meter) treatment groups. In the 178 grams per square meter treatment group, all lesions were noted and in the 89.0 grams per square meter treatment group, all but two lesions (distended gall bladder and hydropericardium) were noted at necropsy (Irwin and Karstad, 1972).

Waterfowl poisoned by lead shot frequently have lesions in heart muscle and muscle of arteries and arterioles. Myocardial infarctions and lesions associated with fibrinoid necrosis of the media of arterioles and small arteries were found in 75 percent of 67 lead-poisoned waterfowl. Also, infarcts were noted in striated muscles and smooth muscles of the gastrointestinal tract (Karstad, 1971).

The first sign of lead poisoning in ducks in usually a marked anorexia and lethargy, probably due to the beginning of the muscle paralysis which follows next. Green staining of feathers from bile occurs late in the lead-poisoning process, often prior to death (Coburn, et al., 1951).

The erythrocyte count normally drops in early stages of lead poisoning in ducks, returns to normal during the intermediate stages of poisoning, and has a rapid decline preceding death. Cells also change to such shapes as dumbbell-, bottle-, sickle-, and tear-shaped forms. The percentage of red cells altered may be as high as 36 percent in acutely poisoned ducks (Coburn, et al., 1951). The levels of delta-aminolevulinic acid dehydratase (ALAD), an enzyme in the biosynthetic pathway for hemoglobin, in the blood of adult mallards on a nutritionally adequate diet and dosed with one number 4 lead pellet decreased to less than 20 percent of ALAD levels in undosed birds (U.S. Department of the Interior, 1976).

Anemia and emaciation are normally found in lead-poisoned ducks, with a total absence of any fatty tissues. Tissues noticeably reduced in size in lead-poisoned ducks include the liver and gizzard muscle (Coburn, et al., 1951).

As with the deposition of lead in tissues of birds and other animals including humans, diet influences the toxic effects of lead (see Section 6.3.2.1). The U.S. Department of the Interior report (1976) reviews research in which toxic effects of lead (including mortalities) were reduced in mallard ducks when they were fed commercial duck ration as opposed to no food or grain diets. The texture of the diet may have some influence on lead toxicity. Longcore, et al., (1974b) showed that the presence or absence of grit, and the type of grit affected toxicity of ingested lead shot. In ducks fed crushed oyster shell grit (contains calcium), a rapid rate of shot erosion was somewhat offset by the concomitant increased chance of voidance of the lead shot. The net result was less, but more rapid, mortality among ducks with grit than in ducks without grit. Anderson and Stewart (1969) found that trace metals, such as lead, are less likely to induce toxic conditions in ring-necked pheasants where calcium is abundant in the soil.

Toxicological symptoms of young Japanese quail fed lead (as lead acetate) at the level of 500 and 1,000 ppm included inhibition of normal growth and anemia.

The performance of juvenile bobwhite quail (Colinus virginianus) receiving up to 1,500 ppm of dietary lead as lead acetate was not significantly influenced during a 6-week experimental period. Feeding 3,000 ppm lead acetate was associated with a significant depression of body weight and an increase in mortality (Damron and Wilson, 1975). Feeding growing quail up to 2,000 ppm lead from either lead acetate or powdered lead or five lead shot per week caused no significant effects upon either body weight or mortality. No significant trends were noted in body weight, feed intake, or organ weight of adult quail that received up to 1,500 ppm lead from lead acetate. Dosing adult bobwhite quail cocks with ten or more lead shot per week caused a significant increase in mortality, and more than 90 percent of those dosed with 30 shot per week died by the end of 4 weeks (Damron and Wilson, 1975).

A few studies have been addressed to the effect of lead on sexual development and reproductive performance in birds. Wetmore (1919) reported that lead may be important in producing sterility in birds that in other respects appeared to have recovered from lead poisoning. Cheatum and Benson (1945) reported that drakes recovering from lead poisoning did not exhibit a significant loss of fertility. Feeding 1500 ppm lead as lead acetate to bobwhite quail did not result in any detectable effect on semen quality (Damron and Wilson, 1975). On the other hand, feeding 500 to 1000 ppm lead as lead acetate to young Japanese quail interferred with normal sexual development in the males (Morgan, et al., 1975). Females may be more sensitive to the effects of lead than males; it has been reported that female Japanese quail exhibited reproductive problems at dietary intakes as low as 1 ppm (Edens, et al., 1976.

Toxicity experiments on chick embryos (Gallus domesticus) revealed that lead chloride is highly toxic, giving survival rates of 74 to 23 percent when used at 0.001 to 5 ppm. Survivors treated with lead displayed a high frequency of anomalies (Birge, et al., 1975).

The end result of the changes caused by lead poisoning is that a bird has little or no intake of nutrients and cannot retain or process nutrients it does have. Protein metabolism and thus, the immune mechanisms, are probably interfered with. In consequence, lead-poisoned birds are subject to both predation and disease (Stickel, 1969). Sublethal doses of lead acetate cause increased mortality in chicks administered bacterial endotoxins (U.S. Department of the Interior, 1976).

5.5 MAMMALS

5.5.1 *Wild*

5.5.1.1 Metabolism: Uptake, Absorption, and Residues--

Investigations have been conducted to evaluate lead contamination in tissues of roadside small mammals, especially mice, and to assess the pathological effects, if any, of lead on these organisms. Small mammals which inhabit roadside areas are exposed to increased levels of environmental lead. In general, it has been found that lead levels in roadside mammal populations are higher than those levels found in populations distant from roadways. Table 5.9 summarizes data from several investigations.

Jefferies and French (1972) found that there is a differential between the concentrations of lead in small mammals of woodland and field areas and those living on roadside verges (see Figure 5.2) and also between those living on the verges of major and minor roads. Although there was a 9.2 times difference in the concentrations in the vegetation of major road verges and field areas (307 to 33.4 ppm, dry weight, respectively), presumably due to surface coating on the former, there was only a 1.7 times (or lower) difference in the concentrations in mammals. Mammals living on verges had a mean of 4.2 ppm, dry weight (1.3 ppm, wet weight) in two species.

Despite greater present-day levels of lead aerosols in the environment, Raymond and Forbes (1975) did not find significant differences in the lead burden of hair from natural wild mice as compared to that obtained from musuem specimens.

Braham (1973) reported that lead in California sea lions (*Zalophus californianus*) was highest in hard tissue and lowest in soft tissue. Lead in bone and teeth ranged from 14.0 to 62.8 ppm and from 11.3 to 15.1 ppm, respectively, whereas, lead in fat and muscle ranged from undetectable to 0.6 ppm and from 0.3 to 3.2 ppm, respectively.

Mierau and Favara (1975) found no evidence of lead poisoning in the wild mice populations which they investigated. Further, the exposure level required to produce recognizable lead poisoning in captive deer mice was about five times higher than that measured in the wild roadside mice populations.

A survey of lead in tissue of Ohio upland game animals has been completed by Lynch (1973). Table 5.10 is from Lynch's study and indicates lead levels in deer, rabbit, and squirrels. Of the muscle tissue analyzed only two samples, one from rabbit and one from squirrel, exceeded 7 ppm.

Table 5.9 MEAN CONCENTRATION OF LEAD IN TISSUE OF SMALL MAMMALS FROM ROADSIDE AND CONTROL SITES
(ppm, dry weight)

Organism	Tissue	Control Site	Roadside Site	References
Deer mouse *Peromyscus maniculatus*	Brain	0.14	<0.57 - 0.84	Mierau & Favara (1975) and
	Lung		<0.58	Welch & Dick (1975)
	Liver	1.06	0.92 - 3.29	
	Stomach		1.64	
	Kidney	3.28	1.87 - 8.46	
	Muscle		0.49	
	Bone	4.84	14.0 - 52.1	
	Whole body	2.7		Schlesinger & Potter (1974)
White-footed mouse (*Peromyscus leucopus*)	Whole body	2.6	4.4	Quarles et al.,(1974)
Meadow vole (*Microtus pennsylvanicus*)	Whole body	4.9	8.6	Quarles et al.,(1974)
Short-tailed shrew (*Blarina brevicauda*)	Whole body	2.6 - 5.4	14.0	Quarles et al.,(1974); Schlesinger & Potter (1974)
Shrew (*Sorex* sp.) Deer mouse (*Peromyscus maniculatus*) Townsend chipmunk (*Eutamias townsendii*) Meadow vole (*Microtus* sp.)	Hair (unwashed)	6.0	235.6	Raymond & Forbes (1975)

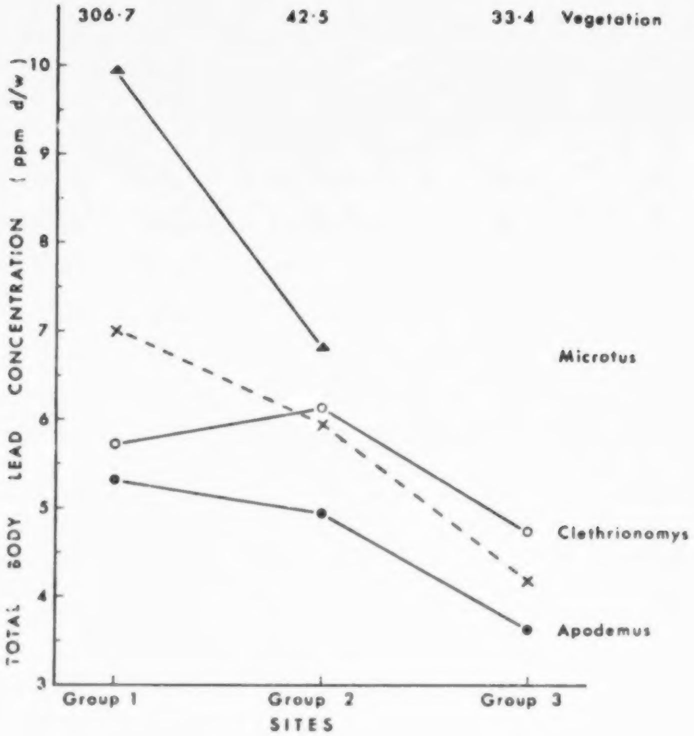

Figure 5.2 The dry weight concentrations of lead in Microtus, Clethrionomys and Apodemus trapped at Group 1 (A1 road verges), Group 2 (minor road verges) and Group 3 (arable and woodland) sites. The broken line joins the means for the three species (two at Group 3 sites). The mean level of lead (d/w ppm) on the vegetation at these sites is also given. Source: Jefferies and French. Reprinted with permission from Environmental Pollution. (c) Applied Science Publishers, Ltd., 1972.

TABLE 5.10 LEAD CONCENTRATIONS IN TISSUE SAMPLES FROM VARIOUS OHIO MAMMALS[a]

Tissue	No. Analyzed	No. Positive[b]	Pb Concentration, ppm, Wet Weight $\bar{X}$±S.D.[c]	Median	Range
			White-Tailed Deer		
Brain	14	6	1.45±1.01	n.d.[d]	n.d.-2.91
Hair	8	6	5.92±5.11	2.18	n.d.-14.4
Kidney	35	33	1.06±1.60	0.32	n.d.-6.27
Leg muscle	26	7	0.95±0.69	n.d.	n.d.-2.37
Liver	24	11	0.74±0.32	n.d.	n.d.-1.34
Metacarpal	38	38	4.82±1.73	4.57	2.49-11.04
			Cottontail Rabbits		
Brain	6	4	9.64±3.52	7.22	n.d.[d]12.22
Embryo	1	1	0.625±0.00	0.625	0.625
Femur	24	24	7.77±2.48	7.91	2.49-11.92
Kidney	40	32	1.35±0.88	0.86	n.d.-3.92
Leg Muscle	22	10	1.92±0.00	n.d.	n.d.-8.63
Liver	16	9	5.92±4.01	2.63	n.d.-16.76
Testes	1	1	0.36±0.00	0.362	0.362
			Squirrels		
Brain	3	2	2.04±1.74	0.536	n.d.[d]3.56
Femur	21	21	7.68±3.07	7.56	2.65-14.16
Kidney	18	15	0.47±0.01	0.235	n.d.-2.92
Leg Muscle	24	7	3.28±4.33	n.d.	n.d.-13.49
Liver	13	4	2.04±1.17	n.d.	n.d.-3.24
Testes	2	2	1.42±0.14	1.47	1.31-1.59

[a] Source: Lynch (1973). Reprinted with permission of the author.

[b] Number of tissue samples with detectable lead concentrations.

[c] Mean ± one standard deviation of tissue samples with detectable lead concentrations.

[d] n.d.-no lead detected. Below detection limit of 0.03 ppm lead.

Mouw, et al., (1975) found that wild rats captured in an urban area had markedly elevated tissue lead, particularly in the major lead-storage tissues (bone and kidney) which was twentyfold higher, as compared to rural rats. The fecal levels were fourfold higher in urban rats (see Table 5.11).

5.5.1.2 Effects--

Bazell (1971) reported that a large portion of animals housed at the Staten Island Zoo suffer from lead poisoning. Bazell suggested that major source of lead to these animals appeared to be atmospheric pollution, although lead paint might also be a factor. The animals affected include leopards, a variety of other cats, snakes, and primates. Those animals kept in outdoor cages had the highest lead burdens. The effects of lead upon those animals at the Staten Island Zoo (incidence of lead poisoning of captive animals at the Bronx Zoo has also occurred) included death, hair loss, paralyzation, and loss of muscular coordination. Although Bazell attributed air pollution as a major source of lead for zoo animals, it seems unlikely in view of the fact that lead poisoning in domestic cats, as opposed to dogs, is exceedingly rare.

Studies of lead poisoning in wild animals at the National Zoological Park, Washington, D.C., indicated a cause-effect relationship between leaded paint and lead intoxication of caged animals (Zook, et al., 1972). Postmortem diagnosis of primates, parrots, and fruit bats indicated that these animals were subjected to lead poisoning.

Changes in several biologic indices (depression of delta-aminolevulinic acid dehydratase in the kidney and red blood cells, presence of renal intranuclear inclusion bodies, and increased kidney weight) confirmed lead-poisoning in urban rats versus rural rats (Mouw, et al., 1975). There were no ovarian cysts or testicular degeneration in the wild rats as has been seen in lead-poisoned laboratory rats (see Section 6.3.2).

Evidence to substantiate the effect of lead contamination on the population dynamics of wild mammals is at present lacking, due no doubt to the extreme difficulty in assessing cause-effect mortality factors which operate upon wild annimals under natural conditions.

5.5.2 Domestic

5.5.2.1 Metabolism: Uptake, Absorption, and Residues--

Lead poisoning generally is considered to be the most common cause of accidental poisoning of domestic animals. The condition is diagnosed most frequently in cattle and dogs (Aronson, 1972). Common histories of exposure in dogs include chewing on objects painted with lead-based paints, eating linoleum, or ingesting lead materials such as shotgun slugs or curtain weights. Case histories indicate that lead poisoning in cattle is usually the result of a single ingestion of a material containing a large quantity of lead (Osweiler, et al., 1973). The major source of lead to domestic stock continues to be lead paints (Buck, 1970 and 1975). Other sources of lead include used motor oil, discarded lead storage batteries and oil fil-

Table 5.11 LEAD CONCENTRATIONS IN TISSUES FROM URBAN AND RURAL RATS[a,b]

	Lead Concentration, ppm				
	Urban		Rural		
Sample Source	No. of Samples	Mean ± SE	No. of Samples	Mean ± SE	Significant Differences, P Value
Blood	39	0.55 ± 0.04	28	0.17 ± 0.02	.001
Liver	21	3.34 ± 0.45	19	0.44 ± 0.09	.001
Kidney	25	22.7 ± 2.8	20	1.14 ± 0.28	.001
Lung	23	1.24 ± 0.20	19	0.24 ± 0.03	.001
Brain	22	1.11 ± 0.17	19	0.21 ± 0.06	.001
Bone	24	200.00 ± 19	18	10.3 ± 1.9	.001
Feces	19	178.00 ± 30	19	46.6 ± 6.0	.001

[a] Source: Mouw, et al. Reprinted with permission from Archives Environmental Health. (c) American Medical Association, 1975.

[b] Data are from 41 urban rats (26 males and 15 females, body weight = 382 ± 13 gm) and 28 rural rats (20 males and eight females, body weight = 322 ± 14 gm).

[c] A large fraction of the lung (10/19) and brain (12/19) samples from rural rats were entered as the minimum detectable concentration (0.2 µg/gm) for these tissues. This manipulation has reduced the apparent SE for these two values and (probably) elevated the mean, but is unlikely to have affected the statistical conclusion.

ters, machinery grease, putty, linoleum, and lead caulking. Poisoning in cattle can also arise from long-term ingestion of crops and/or pasture forage contaminated by lead settling out from fumes and dust emitted from lead- and copper-smelting operations (Aronson, 1972; Dorn, et al., 1974; Dorn, et al., 1975; Orheim, et al., 1974). The latter is the principal transfer mechanism involved in lead poisoning of horses (Aronson, 1971; Knight and Burau, 1973).

Most field investigations of lead contamination of domestic animals have taken the form of comparison of tissue burdens among test animals, those in the vicinity of a lead source, and control animals. Orheim, et al., (1974) found no difference in lead concentration of blood and milk between dairy cattle within the "fallout" zone of a lead smelter versus control cattle. However, lead levels in the hair of the test versus control animals were significantly different. Dorn, et al., (1974) also reported significant lead accumulation in washed bovine hair. Investigations carried out on a test farm exposed to production sources of lead revealed increased concentrations of lead in the milk of test cows as compared to control cows (Dorn, et al., 1975). The highest concentration measured in milk was 0.35 ppm. This figure is close to the maximum of 0.3 ppm reported by Aronson and Hammond (1964) in milk from cows exposed to a high intake of lead.

When Allcroft (1950) fed calves large quantities of lead (0.1 to 0.5 gram per kilogram body weight), there was a marked and rapid rise in the blood lead level and if the animal survived, the lead content of the blood did not revert to normal for many months. When given as the metal or the finely ground ore galena, lead was absorbed to a much smaller extent than when given as the acetate, phosphate, basic carbonate, oxide and wet or dry paint. After the ingestion of the various lead compounds mentioned above, the highest concentrations, by far, were found in the kidney cortex (297 ppm) and liver tissue (126 ppm). Allcroft (1950) considers the kidney cortex content to be of specific diagnostic value.

According to Buck (1975), determination of blood lead concentrations offers the best antemortem evidence for the presence or absence of lead poisoning in cattle. Blood-lead concentrations greater than 0.35 ppm in cattle should be judged as evidence of unusual exposure. Tables 5.12 and 5.13 give background and contaminated lead concentrations in various bovine tissues.

Laboratory experiments which used sheep as the test animal have been conducted. Carson, et al., (1973) maintained sheep on daily regimens of food spiked with 4.5 and 2.3 ppm of lead for 27 weeks. Results showed mean blood-lead levels of 0.30 and 0.17 ppm, respectively, in the two test groups. No clinical signs of lead poisoning in the sheep were observed.

Five groups of foals were fed rations that differed in calcium and phosphorus content for 26 weeks. During the last 15 weeks of the experiments, some of the foals in each ration group were fed 30 ppm lead carbonate daily. The addition of lead at the 30 ppm level significantly increased (P less than 0.05) lead concentrations in whole blood liver, kidney, vertebra, and ribs, but not in metacarpal diaphysis or epiphysis, brain, lung, or muscle. The calcium and phosphorus content of the rations fed did not have a significant influence on whole blood-lead values. In fact, the lead values were highest in the group of foals fed the largest amounts of calcium. The amount of calcium and, to a less extent, phosphorus in the ration had a significant influence on the amount of liver-tissue lead (Willoughby, et al., 1972b). In some cases, the concentration of lead in the livers of foals fed the least amount of calcium and phosphorus were twice as high as values from foals fed greater amounts of these minerals.

5.5.2.2 Effects--

Since lead accumulates in the body, chronic exposure to small amounts of lead may lead to toxicosis in domestic livestock. For cattle, the daily intake of approximately 6 to 7 milligrams of lead per kilogram body weight can result in toxicosis (Hammond and Aronson, 1964). Acute, lethal, single exposures are in the magnitude of 400 to 600 milligrams of lead per kilogram of body weight for calves and 600 to 800 milligrams of lead per kilogram of body weight for adult cattle, (Buck, 1975). These values are influenced by the form of lead ingested and other environmental factors. Allcroft and Blaxter (1950) showed that, in the case of young calves, 0.2 to 0.4 gram of lead (as lead acetate, carbonate or oxide) per kilogram of body weight was sufficient to cause death in a few days. Horses are more susceptible and approximately 2 milligrams of lead per kilogram body weight can lead to lead poisoning (Aronson, 1971). Lead poisoning in domestic animals appears to affect all major organs and organ systems, in particular the central nervous system and the blood vascular system.

Christian and Tryphonas (1971) made gross and microscopic examinations of nine cattle, ranging in age from 3 months to 6 years, affected with naturally occurring lead poisoning of 1 to 32 days' duration. Gross brain lesions consisting of cerebrocortical softening, yellowish discoloration, and cavitation were seen only in cattle with prolonged clinical illness (affected more than 9 days). Tips of most cerebral gyri were affected; lesions were most severe in the occiptal lobes. In cattle with acute poisoning, microscopic lesions varied from diffuse capillary activation to scattered focal areas of status spongiosus and necrosis of the cerebral cortex. In cattle with subacute and chronic poisoning, the microscopic lesions were located at the gyral tips and ranged somewhat from different degrees of status spongiosus, astrocytic swelling, and nerve cell degeneration to severe cavitation and vascular proliferation.

The majority of lead poisoning incidents reported for horses have been attributed to consumption of vegetation contaminated by lead from local mines and smelters. Knight and Burau (1973) researched two incidents of lead poisoning on two horse ranches located within the "fallout" area of a lead smelter. Contaminated vegetation consumed by the horses proved to be the lead source. Symptoms of chronic lead poisoning in the horses was evidenced by anorexia, loss of body weight, muscular weakness, anemia, laryngeal hemiplegia, elevated urine lead concentration following chelation therapy, and inhalation pneumonia preceding death.

Schmitt, et al., (1971) found that excessive amounts (up to 264 ppm) of lead in ingested forage were found to be the primary cause of a debilitating

Table 5.12 "BACKGROUND" BOVINE LEAD CONCENTRATIONS IN TISSUES AND RUMEN CONTENTS[a]

Specimen Analyzed	No. of Samples	Mean Lead Content, ppm, Wet Weight[b]
Blood	92	0.103 (±0.044)[c]
Liver	197	1.12 (±1.36)
Kidney	181	1.21 (±1.69)
Rumen contents	52	1.07 (±1.44)

[a] Source: Buck. Reprinted with permission from Journal American Veterinary Medical Association. (c) American Veterinary Medical Association, 1975.

[b] Data from records of the Iowa State University Veterinary Diagnostic Laboratory, 1967-1970.

[c] Standard Deviation.

Table 5.13 LEAD CONTENT IN TISSUES AND RUMEN CONTENTS FROM CATTLE WITH CLINICAL LEAD TOXICOSIS[a]

Specimen Analyzed	No. of Cases	Lead Content, ppm, Wet Weight[b]	
		Mean	Range
Liver	100	26.40	1.0 - 83.0
Kidney	105	50.30	3.0 - 200
Blood	50	0.81	0.19 - 3.80
Rumen contents	52	400.80	0.0 - 11,875

[a] Source: Buck. Reprinted with permission from Journal American Veterinary Medical Association. (c) American Veterinary Medical Association, 1975.

[b] Data from records of the Iowa State University Veterinary Diagnostic Laboratory, 1967-1971a

disorder in six horses. This represents a daily intake of lead of 5.5 mg/kg based on estimates of forage consumption by horses (Aronson, 1972). Necropsy findings included depletion of adipose tissues with generalized emaciation, edematous synovial membranes, erosive and rough joint surfaces, and exostoses of the articulating bones, especially metacarpals. The more significant histopathological findings were diffus[illegible]ema and necrosis of individual nerve cells, hepatic cell degeneration, and a slight to moderate degree of nephrosis. Many epithelial cells of the collecting renal tubules and some of the nuclei of hepatic cells showed intranuclear inclusion bodies, suggesting the presence of lead.

Groups of young, growing horses were fed toxic amounts of lead only, zinc only and the same amounts of lead and zinc together. Those fed lead only developed pharyngeal and laryngeal paralysis ("roaring") whereas those fed zinc only and lead and zinc together developed the same clinical syndrome which included swelling at the epiphyseal region of the long bones, stiffness and lameness. Animals fed lead only did not become anemic, and weight loss did not occur until after there was an interference in swallowing. Zinc appeared to have prevented the development of clinical signs of lead poisoning in the young, growing horses (Willoughby, et al., 1972a).

Zook, et al., (1969) found that lead poisoning is a common disease of young dogs, especially in the summer and fall. The signs of poisoning were characterized by gastrointestinal dysfunction (colic, vomiting, and diarrhea) and nervous disorders (convulsions, hysteria, nervousness, behavior changes). Their blood consisted of numerous stippled and immature (especially nucleated) erythrocytes in the absence of severe anemia. Clarke (1973) pointed out that there are practically no references to lead poisoning in the cat. The cat is resistant to the absorption of lead in large quantities; however, it succumbs to repeated administration of small doses. In cases where cats were poisoned, they showed both gastric (anorexia, vomiting) and nervous (epileptiform convulsions, dashing about as if mad) symptoms. They were very thirsty, somewhat constipated and partially paralyzed, with hyperaesthesia of the skin. Some degenerative changes were noted in the liver and kidneys. The intestines were contracted and there was a blue color in the tongue and throat.

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6.0 EFFECTS ON HUMANS

6.1 SUMMARY

The metabolism of lead is concerned with uptake and absorption, distribution, transport, elimination, and biological half-life of both inorganic and organic compounds of lead.

Lead may be taken into the body by inhalation, ingestion or percutaneous absorption, and placental transfer. It may enter the respiratory system in the form of particles, gases or vapors. Various estimates place pulmonary retention rates of inhaled lead in the range of 37-50 percent. Because lead alkyls in the air are broken down by light and heat, their presence in the air is transient and it is believed that they contribute little to the inhalation burden. Of greater importance are the inorganic lead compounds emitted by automobiles using leaded gasolines. Under normal conditions, not more than 5 to 10 percent of ingested lead in food is absorbed from the gut. The fraction absorbed from liquids taken between meals may be considerably greater. The amount of lead absorbed from the gut in animals appears to be less than in man. Lead is absorbed mainly from the small intestine, to a lesser extent from the colon, and not at all from the stomach. Skin absorption of lead compounds is of importance only in the case of lead alkyls and lead salts of naphthenic and fatty acids.

Following absorption nearly all the inorganic lead in the blood is associated with the erythrocytes. The bonding sites on the maternal erythrocytes are not saturated. It is then distributed to various tissues and is highest in bone and hair; intermediate in aorta, liver, and kidney; and lowest in heart and brain. In the steady state, more than 90 percent resides as a relatively nondiffusible fraction in the skeleton. The concentration of lead in the bone rises steadily to about the fourth decade, reaches a plateau, and then decreases in many cases in the seventh and eighth decade. Fluctuations in the amount of lead intake, either through inhalation or ingestion cause movements into and out of various compartments of the body lead pool (e.g., hard tissue, soft tissue, pluma, erythrocytes, etc.). Equilibration of the various compartments occurs after a relatively small lead intake is achieved. Only then do lead levels in tissues and fluids accurately reflect body pool.

Exposure to lead through placental transfer of inorganic lead probably has greater potential for injury to the embryo, fetus, and neonate than has exposure during adulthood. Placental transfer of inorganic lead has been widely reported.

Extensive studies of tissue lead distribution have been reported. A detailed investigation of blood-lead levels of male residents in 19 cities in the continental United States showed wide variations from one city to another as did individual values in each city. Concentrations of lead in the aorta have been found to be positively correlated with aorta calcium concentrations. Levels of lead in shed deciduous teeth are elevated in cases of known lead poisoning and in children who reside in areas where lead poisoning is endemic. Lead is normally found in higher concentrations (on a weight per weight basis) in hair than in any other tissue. The high lead content has been found in the hair of city dwellers or those living near a lead smelter as compared to those living in a rural area. Traffic policemen within cities have a higher average lead content in their hair than members of the general population.

The organic lead compounds have no special affinity for bone, but high concentrations may appear in the brain and liver. The metabolism of tetraalkyl lead proceeds via the highly toxic trialkyl lead which in turn is converted to inorganic lead.

The principal routes of elimination of lead from the body are via feces and the urine. Fecal excretion of both inorganic and organic lead is greater than urine excretion. For inorganic lead the ratio in man is about 2:1. The excretion of lead through the kidney is hampered by the high degree of interaction of lead with ligands present in erythrocytes and/or plasma proteins. About 90 percent of the lead in the feces represents lead which has passed unabsorbed through the gut.

Indirect estimates of lead have been made by balance studies in human subjects. Data derived from urine and blood samples of individuals exposed to known concentrations of atmospheric lead oxide have been used to develop mathematical models describing lead uptake and excretion kinetics. Estimates of half-times for lead in bone have varied from 64 days in the spine of rats to 7500 days in the skeleton of a dog. Research continues on the development of a suitable metabolic model which incorporates lead uptake and excretion kinetics for humans exposed to atmospheric lead.

Most of what is known about lead toxicity applies to (1) adults exposed in the industrial setting and (2) children who have ingested large amounts of lead. Symptoms these two groups may exhibit include abnormalities in the blood (red blood cell stippling, anemia, decreased ALAD activity) and in kidney function (glycosuria, hyperphosphaturia and hyperamino aciduria. In addition children are more susceptible to lead encephalopathy with a potentially fatal outcome.

In the last 5 years, increasing emphasis has been placed on the more subtle aspects of lead toxicity which seems to be appropriate considering the nature of contemporary lead exposure. For most individuals, ingested lead is more likely to be derived from water, soil, food, and ambient air than from occupational exposures or industrial emissions.

Lead, like cadmium and mercury, forms mercaptides with the -SH group of cysteine and less stable complexes with other amino acid side chains. This apparently results in an inhibitory action on a number of enzymes. An example is the strong inhibition of lipoamide dehydrogenase, an enzyme crucial to cellular oxidation, by lead (as Pb^{2+}) concentrations as low as 6.5×10^{-6} M. This inhibition probably occurs through binding to the dithiol configuration at the active catalytic center. Activities of several other enzymes (e.g., ATPases, aldolase, glucose-6-phosphate dehydrogenase (G-6-PD), adenyl cyclase, microsomal enzymes, acetylcholinesterase) are affected by lead.

Within the cell, lead has greatest affinity for mitochondrial membranes and nuclei. Altered nucleic acid content (RNA and DNA) of leukocytes have been observed in adult cases of plumbism. Lead binds with an acidic protein fraction to form discrete intranuclear inclusion bodies within the kidney tubule cells of chronically poisoned rats, rabbits, and humans.

The affinity of mitochondria for lead results in morphological and functional alterations which have been verified in various animal species. Mitochondrial accumulation of lead in the kidneys inhibits ADP-stimulated respiration. Impairment of energy metabolism by lead may be responsible for the reduced transport function of the kidney.

Inorganic lead toxicity may give rise to clinical syndromes such as abdominal colic, anemia, acute or chronic encephalopathy, peripheral neuropathy, and chronic nephropathy. Manifestations of organolead poisoning are dominated by the involvement of the central nervous system and differ from inorganic lead toxicity. Absorption of the gasoline antiknock additives, TEL or TML, results in similar symptomatology. The principal manifestations of exposure to TEL are insomnia, asthenia, ataxia, tremors, neuromuscular pain, hallucinations, mania, delusions, and psychosis.

Lead has varying effects on different organ systems. In the kidney, lead interferes with tubular sodium absorption perhaps through marked inhibition of Na$^+$/K$^+$ ATPase in lead-poisoned animals. It also inhibits tubular reabsorption of glucose, and amino acids and phosphate.

The effects of lead on hematopoiesis include two aspects: (1) the influence on circulating erythrocytes resulting in, for example, altered osmotic and mechanical fragility and (2) the impairment of the production of hemoglobin resulting from the effects of lead upon bone marrow.

Heme synthesis is severely affected by lead. This is reflected in the high levels of excreted porphyrin precursors in the urine. One of the most lead-sensitive enzymes involved in heme synthesis is delta-aminolevulinic acid dehydratase (ALAD). A decrease in ALAD activity in mature erythrocytes is a very early sign of lead exposure. ALAD activity decreases exponentially when blood-lead levels increase. The effective threshold is not certain but probably is below PbB = 20 micrograms/100 ml.

Many children living in slum housing have been observed to have elevated blood-lead levels and decreased red cell ALAD levels. Reversal of the ALAD deficit in lead-poisoned erythrocytes has been accomplished with glutathione reductase (GSH) *in vitro* and, to some extent, *in vivo*. Chelation therapy, especially EDTA, also reverses ALAD inhibition.

The immunologic impairment of lead is reflected in its decreasing of the normal Vitamin C content of the adrenal gland. Chronic lead exposure at high doses reduces the effectiveness of the immune system in experimental animals.

No evidence has been forthcoming to implicate any cardiovascular disease in humans following chronic lead exposure. Lead has been found to exert a depressing effect upon the endocrine function of such glands as the thyroid, pituitary, adrenal cortex, and juxtaglomerular apparatus.

Pediatric lead poisoning follows persistent lead ingestion usually over a period of several months. For early recognition of the disease, a high index of suspicion and judicious use of four laboratory tests - blood examination for anemia and erythrocytic stippling; roentgenograms of the long bones for "lead lines"; plain x rays of the abdomen, looking for radiopaque flecks within the intestine; and a urinalysis especially checking for coproporphyrinuria - are indicated.

A positive correlation has been reported between mental retardation and high levels of lead in drinking water. One study showed that as levels of lead increased, general cognitive, verbal and perceptual abilities decreased in a group of preschool children.

Lead ingestion in children has been linked to minimal brain dysfunction or "hyperkinesis". One study reports an association between hyperactivity and raised lead levels. A large body-lead burden may exact consequences that have been hitherto unrealized. Sensitive techniques now available in the behavioral and neurosciences are being used to detect altered motor activity, motor performance and other previously undetectable abnormalities in these animal models.

Chelation therapy is the method of choice for treating plumbism in the United States. The three chelating agents used are edathamil calcium disodium (CaEDTA), 2, 3-dimercaptopropanol (BAL), and d-penicillamine (PCA). CaEDTA administered intramuscularly evokes a great increase in lead excretion in children and adults with high lead exposure. In adults with mild plumbism, parenteral CaEDTA is the most effective of the chelating agents.

A study of chromosomal abnormalities in lead workers showed that those having blood-lead levels of 62 to 88 micrograms per 100 ml had gap-break type aberrations of chromatids and increases in tetraploid mitoses and the mitotic index.

Severe lead intoxication has long been associated with sterility, abortion, stillbirths, and neonatal deaths in man and other animals. Litter size, embryonic growth, and fetal development have been reduced in laboratory animals by inorganic lead. Damage to reproductive organs and interference with estrus cycles by inorganic lead have also been noted. Men occupationally exposed to lead have been reported to exhibit substantial increases in spermatogenic abnormalities (asthenospermia, hypospermia, and teratospermia).

Teratogenic effects of inorganic lead in animals are manifested by cogenital skeletal malformations. Human fetuses *in utero* may be a group at particular risk because inorganic and organic lead cross the placenta. One human case has been noted where the mother, exposed to illegal whiskey containing lead, gave birth to an infant with neurological defects, intrauterine growth retardation, and postnatal failure to thrive.

Renal, adrenal, thryoid, prostate, and pulmonary adenomas, renal adenocarcinomas and testicular carcinomas have been found in rats and mice given lead phosphate, lead acetate, and basic lead acetate via dietary and/or parenteral routes. Lymphomas have been found to result from the subcutaneous injection of TEL. By contrast, epidemiological evidence to date does not indicate that lead has a similar carcinogenic effect in humans.

As in the toxicity of other materials, factors such as dietary calcium, phosphorus, copper, protein, and Vitamin D, season of the year, drugs, and exposure to other metals can alter severity of intoxication.

Epidemiological surveys in normal adults indicate mean blood-lead levels are approximately 20 micrograms per 100 grams of whole blood (range 5 to 30 micrograms per 100 grams whole blood). Persons in daily occupational contact with motor vehicles in confined spaces show blood-lead levels in the 40- to 50-microgram range.

Epidemiologic studies of blood-lead levels in general and occupational groups show a logarithmic regression on estimated atmospheric exposure. Experimental results at the same and higher levels show a dose-reponse relationship which fits the same regression. The data imply that long-term increases in atmospheric lead will result in progressively smaller incremental increases in blood lead per unit increase in air lead concentration.

Orchardists and their children in the Wenatchee area of Washington State, who had been exposed to lead arsenate were examined for toxicological effects of lead. In the orchardists, both blood- and urine-lead concentrations ranged from slightly higher to the same values as controls. Studies on the children indicated that their urinary lead and arsenic concentrations were nearly twice as high as those of a control group. There was no indication of adverse effects of lead arsenate exposure on the health of the Wenatchee orchardists or their children.

Average blood-lead levels in adults living near heavily-traveled freeways in Los Angeles County were substantially higher than those found in adults living near the ocean, or at least 1.6 kilometers (1 mile) from the freeway. However, the high blood-lead levels were similar to other Los Angeles populations and lower than those reported for some other urban populations.

Poor personal hygiene and play habits of children living in areas where the lead content of house dust, outdoor dust, and soil is considerably elevated from, for example, a secondary smelter, can result in excessive lead absorption. However, the increases recorded do not appear to cause clear-cut symptoms of lead poisoning. It is uncertain whether or not subtle neurological changes occur from such exposure.

The Seven-City Study showed a positive, but not a significant correlation between average blood-lead levels and average annual airborne lead exposures ranging in concentration from 0.17 to 3.39 micrograms per cubic meter. Although extensive, the study was inconclusive on this point because air samples did not accurately reflect air lead exposure of the subjects.

The life expectancy of lead workers in an environment in which occupational exposures to lead were controlled in conformity to currently recommended environmental and biologic standards was approximately the same as that of all U.S. males.

Slowed nerve conduction has been observed in storage battery factory workers whose blood-lead levels had never exceeded 70 micrograms per 100 milliliters of blood. There were no signs of functional neuromuscular disturbances, however.

Fragmentation of bullets during firing, explosive vaporization of primer, and aerosolization of lead suboxide particles during bullet molding appear to have been the major sources of mild lead poisoning among instructors at an indoor pistol range.

Epidemiologic features of excessive lead absorption in children include prevalence of pica in preschool children, seasonal variation, age distribution of cases, association with dilapidated and deteriorating houses and race. Today in the United States, plumbism in children is believed to be due almost entirely to the repetitive eating of leaded house paint. The interior woodwork, painted plaster, and wallpaper of houses built prior to 1940 may contain layers of flaking lead-pigment paints which have never been removed. Several such flakes may contain far more than the average permissible (300 micrograms) daily intake of lead.

At least 600,000 U.S. children reportedly have high levels of blood lead. In 1971 a survey in 27 cities showed that 21 percent of inner-city children had symptoms of excessive lead exposure. As many as 2.9 million American children might run the risk of lead poisoning.

The maximum daily permissible intake (DPI) of lead from all sources without excessive body lead-burden in children has been considered to be 300 micrograms. The DPI should preclude increases in the total body burden of lead in children between 1 and 3 years of age as well as in older children. This DPI was based on the assumption that lead absorption in children is similar to absorption in adults, a presumption which has recently been shown to be incorrect.

In children, blood-lead levels less than 40 micrograms of lead per 100 grams of whole blood are assumed to indicate negligible risks with normal daily dietary intake accounting for most of the ingestion. The biological significance of 50 to 80 micrograms of lead per 100 grams of blood is unclear. Levels greater than 80 micrograms of lead per 100 grams of blood signify an unacceptable risk to health. Early studies in New York City indicated that lead poisoning in children results in death in about 15 to 20 percent of the cases, and neurological and mental disturbances from encephalopathy in 25 percent of the cases. The apparent increased incidence of lead poisoning (comparison of 1964 with 1954) is believed due to the vigorous case-finding programs that resulted in the discovery of cases in the asymptomatic state prior to the onset of encephalopathy. Encouraging was the sharp decrease in the number of deaths (8 percent in 1964).

The screening in New York City in 1971 of 100,000 children, age 1 to 6 years, showed that 2 percent of these children had blood levels of 60 micrograms or greater. Significant elevated blood-lead levels were found three times more often among black children than among Puerto Rican children. Seasonal variations of blood-lead levels showed a summer peak. The New York City results are typical of lead studies in inner-cities having old and dilapidated housing that accentuate the lead paint problem.

The principal cause of elevated lead in dirt around frame houses in selected urban areas has been attributed to lead paint on these houses. Using a naturally occurring tracer lead isotope, dust, and air-suspended particulate were found not to be the sources of elevated lead body burdens of children residing in these areas.

Deleterious health effects, for example, mental disorders and school performance, as evidenced by psychological referrals and problems of attention and concentration, were observed in children who were treated for severe lead poisoning and in children without diagnosed lead poisoning who had elevated blood-lead (over 50 micrograms) levels.

6.2 METABOLISM

6.2.1 Uptake and Absorption

6.2.1.1 Inhalation--

Besides the free lead ion, the inorganic lead products include such industrially used compounds as the acetate, arsenate, carbonate, chloride, chromate, oxides, suboxides and the sulfate. Industrial lead poisoning usually results from inhalation of aerosol lead emitted in the form of dust, fume, mist, or vapor. When inhaled, the small lead particles (less than 1 to 2 micrometers in diameter) tend to be retained by the respiratory tract to be absorbed or coughed up and swallowed later.

Kehoe (1961a,b; 1964) studied the deposition of lead sesquioxide in the human respiratory tract, using particles with mass median equivalent diameters (MMED) of 0.25 and 2.9 micrometers. The deposition of the smaller particles was 36 percent and was 46 percent for the larger particles. Mehani (1966) found deposition values ranging from 39 to 47 percent, but unfortunately failed to determine particle size. Hursh and Mercer (1970) assessed the percentage of lead deposited after inhalation of natural aerosols on which lead-212 was adsorbed. They found a range of 27 to 62 percent, which was dependent on particle size.

Rabinowitz, et al., (1974) calculated the quantity of lead absorbed from a typical urban atmosphere (lead concentration equals 1 to 2 micrograms per cubic meter) to be 15 plus or minus 3 micrograms per day.

Bingham (1970), using a technique of harvesting alveolar macrophages from excised mammalian lungs, found that rats inhaling minute quantities of lead sesquioxide (10 and 150 micrograms per cubic meter) for periods of 3 to 12 months showed a temporary decrease in the number of cells compared with rats inhaling filtered air (0.1 microgram per cubic meter). The functional significance of this effect and the applicability to humans is unknown.

Macrophages probably do play a role in respiratory uptake of lead in humans. The rapid absorption from this route noted by Chamberlain, et al., (1975) is possibly a result of phagocytosis. This route of entry causes lead to enter directly into the blood stream.

By phagocytosis and other routes, inhaled lead eventually reaches the bloodstream. Coulston (1973) and Knelson, et al., (1973) describe a study in which twenty human volunteers were exposed to 10.9 micrograms per cubic meter of lead sesquioxide 23 hours per day for 4 months (see Figure 6.1). In the exposed group the blood lead concentration increased to nearly twice their pre-exposure levels while the level remained relatively unchanged in the controls. During the final six weeks of the experiment, there was no apparent increase in the blood lead of the exposed men, the level remaining at about 35 micrograms per 100 milliliters of blood. After about 6 weeks of exposure the ALAD activity had decreased to about one-half the pre-exposure value in the men (see Section 6.3.2.2).

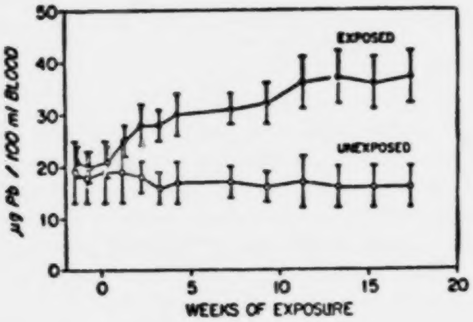

Figure 6.1 Levels of blood lead in volunteers exposed to 10.9 micrograms per cubic meter lead sesquioxide.
Source: Coulston. Reprinted with permission from Environmental Quality and Safety, Vol.2., F. Coulston and F. Korte (eds.), (c) Academic Press, Inc., 1973.

Data from the investigation by Knelson, et al., (1973) on the biological effects of long-term human exposure to airborne lead was used to prepare a mathematical model of the kinetics of respiratory lead uptake. Adult male subjects were subjected to two 18-week exposures at mean lead concentrations of 10.9 plus or minus 3.1 micrograms per cubic meter and 3.2 plus or minus 0.6 micrograms per cubic meter. Baseline blood-lead concentrations before exposure began were 19.6 plus or minus 4.8 micrograms per deciliter. These investigators found that increases in total blood lead observed at the two levels of exposure were closely related to the logarithm of the body burden (see Figure 6.2). A mathematical model was developed which enables one to compute the relationship between total lead and potential increase in body burden. From this relationship, distribution between two theoretical compartments with rapid and slow turnover can be inferred. About 90 percent of the total body burden is believed to go into a slow compartment. Substantial increases in blood lead are forecasted even for respiratory doses well below those commonly encountered in ambient air. Towards the end of the actual exposures approximately 10 percent of the potential increase in body burden might show as increased total blood-lead content.

Experimental studies of prolonged exposure to artificially generated lead aerosols have been reported by Griffin, et al., (1975). The lead aerosol employed resembled that of ambient air in size but differed chemically. Subjects were exposed for 23 hours a day to lead levels of 3.2 and 10.9 micrograms per cubic meter. The experiments were continued for over 4 months to allow time for equilibration of blood lead to the new exposure levels. The exposures resulted in respective increases of 2.0 and 1.4 microgram per 100 ml of blood per 1 microgram per cubic meter in air.

6.2.1.2 Ingestion--

The absorption of lead in the intestine has also been shown to be increased by high fat, low protein and high protein diets, and to be decreased by high mineral diets (Barltrop and Khoo, 1975). Similarly, an extensive review by Karhausen (1973) suggested that other important factors determining absorption include: (1) the chemical form of the lead ingested, (2) dietary calcium level; (3) vitamin D intake; (4) dietary composition; (5) load of lead; and, (6) gastric acidity. Generally, the uptake of lead from the gut is less complete than it is from the lungs. Kehoe (1961a), in a detailed investigation of lead metabolism, found that net absorption of lead from the gastro-intestinal tract is approximately 10 percent in normal adult subjects.

In humans, lead is absorbed mainly from the small intestine, to a lesser extent from the colon, and not at all from the stomach. The coefficient of intestinal absorption is about 0.08 in adults and has been reported to be as high as 0.53 in some children (Alexander, et al., 1973).

Rabinowitz, et al., (1975) used stable isotope and balance studies to investigate the human uptake of dietary and atmospheric lead. Four healthy adult males were maintained in a hospital metabolic unit for periods up to six months with controlled diets and environments. The subjects ate constant diets which were low in lead content but supplemented with stable isotopes of lead, which served as a nonradioactive tracer distinct from other (atmospheric and internal) sources of lead.

The alimentary absorption rates of both the lead nitrate tracer and food

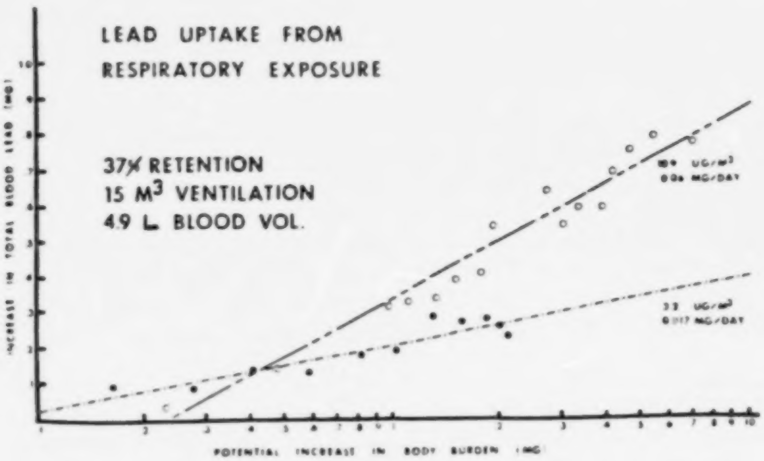

Figure 6.2 Semi-log plot of increase in total blood-lead content and potential increase in body burden. Adapted from Knelson et al.,(1973).

lead varied among the individuals from 6 to 14 percent. Absorption rates as high as 50 percent were seen when lead nitrate or sulfide were administered while fasting. The presence of food in the gut inhibited lead absorption by up to eightfold. Perhaps substances within food compete with lead for absorption sites or perhaps unabsorbable portions of food bind the lead. The data obtained in this study show that gastrointestinal absorption of lead salts is not a simple function of lead intake, but varies among subjects and depends on chemical form.

Reduction of dietary calcium increases the absorption of lead and cadmium (Fleischman, et al., 1968; Six and Goyer, 1970). The great demand for calcium in children, and pregnant and lactating women will cause high calcium absorption rates which may decrease the absorption of lead. Six and Goyer (1972) showed that lowering dietary iron increases lead absorption. Low protein increased lead uptake (Milev, et al., 1970, cited in Waldron and Stofen, 1974; see Section 6.3.3 and Table 6.15).

The availability of lead in a paint film is of special concern in regard to the hazard of lead base paint in children. Gage and Litchfield (1969) have shown that the absorption of lead naphthenate is reduced by half as a result of its incorporation into a dried paint film. Similarly, Kneip, et al., (1974) have shown in monkeys that lead octoate in ground paint is only about one-third as readily absorbed as lead octoate independent of the paint matrix.

The absorption of various salts of lead has recently been studied in some detail (Barltrop and Meek, 1975). Various lead salts showed similar degrees absorption, but metallic lead (180-250 mm diameter) was absorbed only about 14 percent as well as lead acetate. This is of some importance in the evaluation of the contribution made to dietary lead by the small particles of lead solder found in the side seam region of metal cans (Barltrop and Meek 1975).

Experimental studies suggest that absorption of lead is age-dependent. Kostial, et al., (1971a,b) observed that neonate rats have a higher absorption of lead when compared to adult rats. This may be related to the higher absorption of calcium in young rats. In animals, the amount of lead absorbed from the gut appears to be less than in man and the form in which it is administered does not appear to affect its absorption (Forbes and Reina, 1972).

Gruden and Stantic (1975) studied the in vitro transfer of ^{203}Pb through the wall of the duodenum, jejunum and ileum in 6- and 26-week-old female, albino rats. Lead transport through, and lead uptake in the wall were practically the same in all segments. No influence of age on these parameters of lead metabolism was observed. In contrast, these investigators cite research in which very young rats (5 to 7 days old) were found to absorb over 50 percent of applied lead, a figure fifty times larger than observed with 16-week old rats.

6.2.1.3 Percutaneous Absorption--

Penetration of lead through intact skin has not been studied extensively. There are some data suggesting that inorganic lead salts are not absorbed significantly by this route (Lang and Kunze, 1948). A case report, however, by Hamilton and Hardy (1974) notes percutaneous absorption of inorganic lead resulting from the application of a theatrical grease paint which contained 40 percent lead oxide. Lead soaps used in industrial lubricants, however, are absorbed to a significant extent (Hine, et al., 1969).

6.2.1.4 Placental Transfer--

The inorganic forms of lead have a greater potential for injury to the embryo, fetus, and neonate than to the mature adult. Placental transfer of inorganic lead has been reported (Scanlon, 1971; Harris and Holley, 1972; Blanchard, 1966; Palmisano, et al., 1969). Cord blood was found to have lead in concentrations approximating those found in maternal blood (Scanlon, 1971; Harris and Holley, 1972 and Rajegowda, et al., 1972). Scanlon (1971) has found lead concentrations as high as 39 micrograms per 100 milliliters in the umbilical cord of infants in an urvan environment.

Barltrop (1969, cited in Waldron and Stofen, 1974), in a study of normal humans, found that placental transfer of lead began as early as the twelfth week of gestation and that the lead content in fetal tissues increased throughout pregnancy. Fetal bone was found to have the highest tissue-lead level (80 micrograms per gram). Lower lead levels were found in the placenta, heart, kidney, liver, and blood. The total amount of lead transferred per day during pregnancy appeared to be less than 303 micrograms.

Chaube, et al., (1972) detected lead in two-thirds of first trimester human embryonic and fetal specimens. The fifty embryos and fetuses ranged in age from 31 to 261 days gestation. In fetal tissues, lead was found in 77 percent of the liver samples, 15 percent of the brain samples, and 30 percent of the kidney samples analyzed. In the embryos the concentration of lead ranged from 0.38 to 2.0 micrograms per gram of wet tissue. Only two fetuses had detectable lead in the brain. In the liver, the concentration ranged from 0.84 to 4.04 micrograms per gram of wet tissue, and in the kidney from 0.9 to 2.3 micrograms per gram of wet tissue.

The blood of neonates contains lead in concentrations similar to that in cord blood (Kubasik and Volosin, 1972). This is supported by Schroeder and Tipton (1968) who found lead in significant concentrations in neonates of several nationalities (including stillbirths), indicating considerable placental transfer (see Table 6.1).

Haas, et al., (1973), cited by the Task Group on Metal Accumulation (TGOMA, 1973) reporting on 294 sets of maternal and fetal blood samples, found maternal lead levels to average 16.9 micrograms per 100 milliliters, with fetal lead levels averaging 15 micrograms per 100 milliliters. The correlation coefficient between maternal and newborn blood levels was 0.57, which is substantial.

Finklea, et al., (1972, cited in TGOMA, 1973) found that lead is bound to and crosses the placenta. Fetal blood levels were lower than maternal levels, with erythrocytes showing a greater differential than whole blood.

Table 6.1 TISSUE LEAD CONCENTRATION IN CHILDREN AND ADOLESCENTS[a]

Place of Origin	n	Aorta	Liver	Kidney	Pancreas	Lung	Testis	Heart	Brain	Spleen	Bone
		Mean Lead Concentration, ppm ash									
America											
Stillborn	22	65	53	38	-	18	-	25	10	37	-
0-19	23	24	74	62	31	18	9	5	0	10	2
Africa	5	-	100	39	18	23	-	0	13	-	-
India	9	82	100	90	44	68	76	33	10	50	10
Japan	3	27	64	98	26	34	72	15	13	23	27

[a] Source: Schroeder and Tipton. Reprinted with permission from Archives Environmental Health. (c) American Medical Association, 1968.

6.2.2 Transport and Distribution

Following absorption nearly all the lead in the blood is associated with the erythrocytes. It is then distributed to various tissues with concentrations being highest in bone and hair; intermediate in liver, kidney, and aorta, and lowest in heart and brain. Schroeder and Tipton (1968) have observed that in or near a steady state of lead retention in the human body, more than 90 percent resides as a relatively nondiffusible fraction in the skeleton. The body tends to reject lead at a rate commensurate with the rate of ingestion. Therefore, both the blood and urine lead levels vary as a function of the amount of ingested lead. Since only about 10 percent of the ingested lead is absorbed into the body, lead concentrations in the feces reflect short-term fluctuations in lead ingestion, while the urine and blood levels are more indicative of lead ingestion over long periods of time.

Within the blood, lead is associated with the erythrocytes or the plasma proteins, and a small quantity is in a free, ionized state. Approximately 95 percent of the lead in the circulating blood is attached to the red cell. This percentage, however, is dose-dependent and subject to interpersonal variations, according to a review by Waldron and Stofen (1974). The rate of lead uptake by the erythrocytes from the plasma is temperature-dependent as well, according to Clarkson and Kench (1958).

Since lipid-free stroma does not bind lead effectively, the lipids and lipid proteins in the cell membrane seem to act as strong lead binding sites (Vincent, 1958, Teisinger, et al., 1958; see Section 6.3.1). The fact that lead is bound to plasma proteins is not surprising since other heavy metals like mercury and cadmium also show a strong affinity for ligands such as phosphates, cysteinyl and histidyl side chains of proteins, purines, pteridines, and porphyrins (Vallee and Ulmer, 1972). Suggestions for the manner in which lead is bound to the erythrocyte reviewed by Waldron and Stofen (1974) include a peptized lead phosphate sol, a colloidal lead phosphate, a diglyceryl phosphate, mixed salts with calcium and chloride, and a protein-phenolic complex. The affinity of lead toward sulfhydryl (SH) groups suggests a series of reactions on the membrane which lead to a S-Pb-S complex (Passow and Tillman, 1955).

Barltrop and Smith (1971) have reexamined the lead-binding properties of human erythrocytes with respect to the cell fraction in which binding occurs. Their results suggest that lead is bound to the cell contents rather than to stromal material. This was confirmed by the absence of significant binding of lead when washed stroma replaced hemolyzed erythrocytes. These were some indications that the lead was bound to both hemoglobin and some low molecular weight material.

Lead disappears from the blood at a rate which indicates first-order reaction kinetics and may be the sum of three exponential functions (Castellino and Aloj, 1964). Stover (1959) concluded that lead rapidly transferred to the extravascular spaces from the plasma as the latter level declined. To maintain dynamic equilibrium between red-cell and plasma lead, on the one hand, and extracellular and intracellular lead on the other, it is suggested that the ionic fraction of the plasma lead is transferred slowly to other body compartments.

A similar rationale applies to the lead concentration in urine, with blood showing a somewhat lesser fluctuation than urine (Kehoe, 1961a-d).

Extensive studies of soft-tissue lead distribution have been reported by Schroeder and Tipton (1968), and their colleagues (Schroeder and Balassa, 1961; Tipton and Cook, 1963; Tipton and Shafer, 1964; Tipton, et al., 1965) and their data confirmed by Barry and Mossman (1970). Tables 6.1 and 6.2 show the variations in lead tissue concentrations with geographical origin. In general, the aorta has the highest concentration followed by the liver and kidney. The brain and the heart show consistently low values.

Schroeder and Balassa (1961) and Schroeder and Tipton (1968) found that concentrations of lead in the soft tissues, for example, kidney, pancreas, liver, lung, and aorta increase with age up to age 40-50, the rise being particularly sharp in the aorta (see Figures 6.3 through 6.7).

Age-linked accumulations of lead in tissues of Americans were also found for larynx, trachea, and prostate (Schroeder and Balassa, 1961). In aortas collected at autopsy from 18 male residents of Baltimore the highest aortic levels of lead were found in those persons 38 years or older (Poklis, 1975). The lead content of the trachea at autopsy from 17 Baltimore residents sampled in 1972 ranged from 0.6 to 8.8 micrograms per gram of fresh tissue (Poklis and Freimuth, 1975). Contrary to the observation of Schroeder and Tipton (1968), no significant correlation of tracheal lead and age was demonstrated by these data. The mean tracheal lead concentration of the samples collected in 1972 was compared with the mean lead concentration of Baltimore residents reported in 1957. From the increase in tracheal lead, it may be concluded that from 1957 to 1972 there was an increase in the lead "body burden" of Baltimore residents. While the increase may not have been sufficient to affect public health of Baltimore residents, it does reflect an increase in lead exposure in the Baltimore environment.

Bone contains approximately 90 percent of the total body burden of lead which is deposited in the form of the insoluble tertiary lead phosphate. Data by Schroeder and Balassa (1961) and Schroeder and Tipton (1968) indicate that the concentration of lead in the bones rises steadily to about the 4th decade, reaches a plateau, and then decreases in the 7th or 8th decade (see Table 6.3 and Figure 6.8).

Barry and Mossman (1970) and Barry (1973) concluded that there is no decrease in bone lead with old age and suggested that the drop reported by some of the earlier investigators was due to the small number of samples. This confirms earlier work by Morris (1940) who found positive correlation coefficients between age and lead concentration in femur, ribs, and vertebrae with values of 0.48, 0.36, and 0.28, respectively. He concluded that more lead was stored in the long bones than in either ribs or the vertebrae, although there is not a general consensus as to which contains the greatest concentration of lead. Holtzman (1963) demonstrated that the concentration of lead-210 was higher in trabecular than in cortical bone. The lead in the skull bones seemed to be most representative of the mean for the total

Table 6.2 VARIATION IN HUMAN SOFT TISSUE LEAD CONCENTRATION WITH GEOGRAPHICAL LOCATION[a]

Place of origin	N	Aorta	Liver	Kidney	Pancreas	Lung	Testis	Heart	Brain	Spleen	Bone
		Mean Lead Concentration, ppm ash									
Nine American cities	150	140	130	98	49	47	12	5	5	27	43
San Francisco	27	220	160	54	65	38	20	10	5	44	-
Switzerland	9	32	59	45	42	32	23	14	5	20	-
Africa	54	71	64	36	24	28	29	5	5	21	-
Middle East	37	140	70	62	34	42	32	24	14	40	26
Far East	74	91	97	63	39	43	35	19	10	33	30

[a] Source: Schroeder and Tipton. Reprinted with permission from Archives Environmental Health. (c) American Medical Association, 1968.

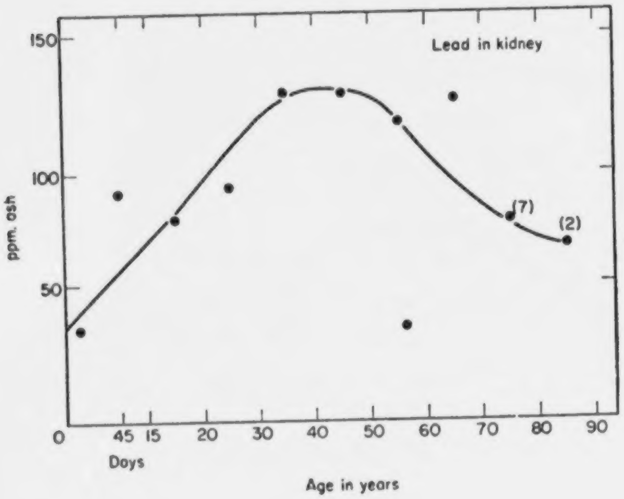

Figure 6.3 Change in concentration of lead with age in kidney. Numbers in brackets in this and Figs 6.3-6.7 indicate number of cases in that decade when <9.
Source: Shroeder and Balassa. Reprinted with permission from Journal Chronic Diseases. (c) Pergamon Press, 1961.

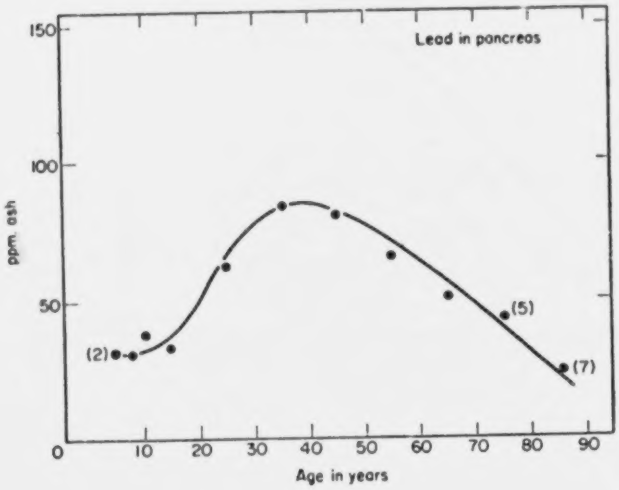

Figure 6.4 Change in concentration of lead with age in pancreas.
Source: Shroeder and Balassa. Reprinted with permission from Journal Chronic Diseases. (c) Pergamon Press, 1961.

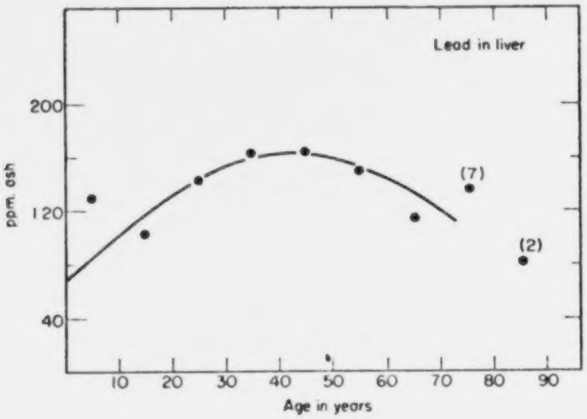

Figure 6.5 Change in concentration of lead with age in liver.

Source: Shroeder and Balassa. Reprinted with permission from Journal Chronic Diseases. (c) Pergamon Press, Inc. 1961.

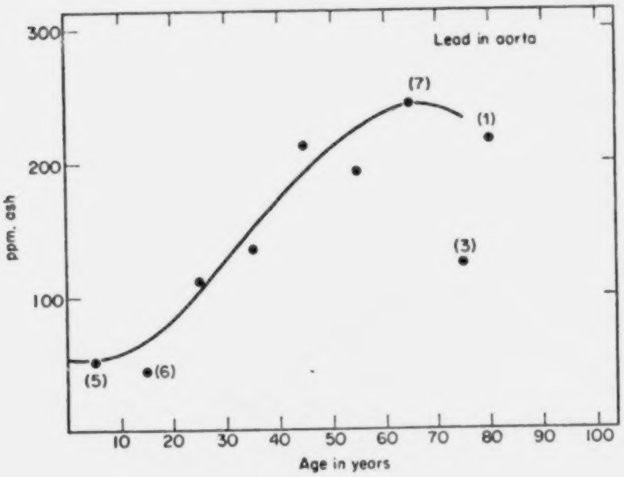

Figure 6.6 Change in concentration of lead with age in aorta.

Source: Shroeder and Balassa. Reprinted with permission from Journal Chronic Diseases. (c) Pergamon Press, Inc., 1961

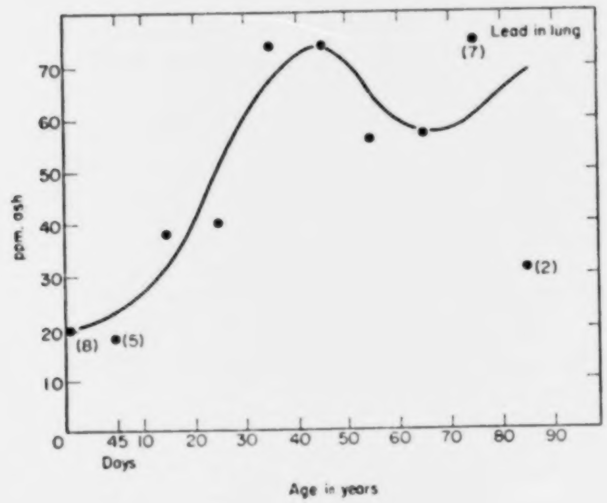

Figure 6.7 Change in concentration of lead with age in lung.

Source: Schroeder and Balassa.
Reprinted with permission from Journal of Chronic Diseases. (c) Pergamon Press, Inc., 1961.

Table 6.3 VARIATION IN BONE LEAD CONCENTRATION WITH AGE[a]

Age, years	n	Mean Lead Concentration, µg/g ash
0-1	4	<1-0
1-9	2	2-5
10-19	9	11-3
20-29	11	16-8
30-39	27	43-1
40-49	9	37-2
50-59	9	31-2
60-69	5	34-2
70-79	2	10-0
80+	1	22-0

[a] Source: Schroeder and Tipton. Reprinted with permission from Archives Environmental Health. (c) American Medical Association, 1975.

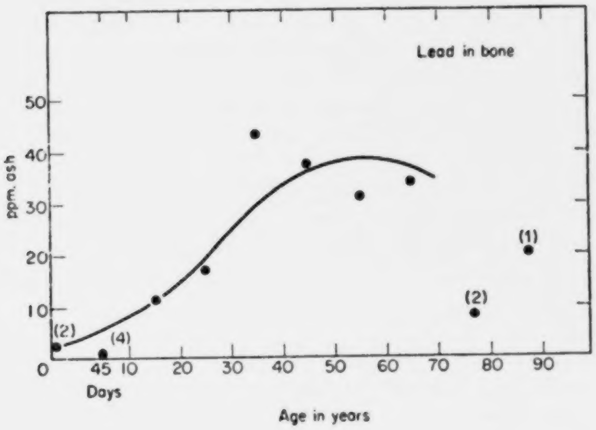

Figure 6.8 Change in concentration of lead with age in bone.

Source: Schroeder and Balassa. Reprinted with permission from Journal Chronic Diseases. (c) Pergamon Press, Inc., 1961.

skeleton. Rib concentrations deviated most from the mean and concentrations in the tibia were very low.

Gross, et al., (1975) assayed 29 tissues per individual from autopsies of 46 white males ranging in age from 20 to 84 years (see Table 6.4). Of the 46 individuals reported, 43 had normal blood-lead concentrations of 40 micrograms per 100 milliliters or less; two individuals had slightly elevated blood-lead concentrations (43 micrograms and 41 micrograms per 100 milliliters); and one had 106.5 micrograms per 100 milliliters. On a wet-weight basis (see Table 6.4), calcified tissues (bones and aorta) contained the highest concentration of lead; the glandular tissues (liver, kidney, and pancreas) were intermediate; and the remaining tissues (which were mostly of a nonglandular nature) had the lowest concentrations of lead. Table 6.5 shows the distribution of lead in the bones and aorta. The low lead values for the bones of the individual in the 5th decade may reflect a chance selection of individuals with low lifetime lead exposures. A rapid increase of lead in the aorta was found after the 5th decade.

Gross and Pfitzer (1975) found that concentrations of more than 2 micrograms per gram of lead in the aorta were associated with severe atherosclerosis involving calcium deposits. As reflected in the skeletal lead, the overall body content of lead increased with age, but many soft tissues did not change and several decreased in lead concentrations with age. The lead content of the liver, kidneys, pancreas, jejunum, stomach, and adrenals decreased significantly with a trend for lead in the blood, skin, cecum, and bladder to decrease as well.

In an assay of the tissues of 129 human postmortem subjects, Barry (1975) found that the tissues of men contained about 30 percent more lead than the tissues of women. Lead increased with age in bones in both sexes but not in most of the soft tissues. Children had lower lead concentrations than adults irrespective of sex. Over 90 percent of the adult burden of lead was in the bone, of which over 70 percent was in dense bone. Occupationally-exposed men aged 55 years or more had mean bone burdens of lead of 595 milligrams compared with 205 milligrams in unexposed men of similar age. Their soft tissue burdens were 16 and 8.5 milligrams, respectively. The cortex and basal ganglia of the brain of males with no known occupational exposure to lead had mean lead levels of 0.10 and 0.09ppm, respectively. The respective concentrations in females were 0.12 and 0.11 ppm. Men aged 29 to 82 years occupationally exposed to lad had mean lead levels of 0.65 and 0.29 ppm, respectively, in the cerebral cortex and basal ganglia. The data for exposed subjects compared favorably with that of Gross, et al., (1975). Hair concentrations did not seem to provide a useful index of lead absorption.

Sumino, et al., (1975) determined the amounts of fifteen heavy metals in fifteen male and fifteen female Japanese cadavers (average weight 55 kilograms, average age 39 years). The highest level of lead was found in the adrenal glands (1.2 plus or minus 0.79 ppm). The average lead content of the female tissue was higher than in male tissue, except in the liver. Significant differences were found in small intestine (P equals 0.01), lung, brain, adrenal glands, and spleen (P equals 0.05). No difference with ages

Table 6.4 TISSUES RANKED ON THE BASIS OF OVERALL MEAN CONCENTRATIONS OF LEAD[a,b]
ppm, wet-weight basis

Tissue	N	X/SD	r	Tissue	N	X/SD	r
Tibia	45	14.09/11.22	0.53[c]	Thyroid	40	0.17/0.11	0.30
Skull	44	13.81/9.09	0.50[c]	Testes	43	0.15/0.09	-0.26
Rib	45	7.14/4.19	0.38[d]	Jejunum	45	0.12/0.05	-0.30[d]
Vertebrae	44	4.42/2.52	0.21	Brain, grey	39	0.11/0.05	-0.18
Aorta	45	1.65/1.82	0.52[c]	Brain, white	41	0.11/0.04	-0.09
Liver	45	0.98/0.53	-0.34[d]	Fascia	43	0.11/0.05	-0.05
Nodes	41	0.86/0.93	0.15	Stomach	45	0.10/0.05	-0.32
Kid. cor.	45	0.79/0.42	-0.53[c]	Bladder	43	0.09/0.04	-0.02
Kid. med.	44	0.48/0.22	-0.38[d]	Skin	43	0.08/0.03	-0.11
Pancreas	45	0.46/0.23	-0.45[c]	Heart	43	0.08/0.04	-0.12
Spleen	43	0.33/0.15	-0.02	Cecum	45	0.07/0.03	-0.07
Lung	42	0.36/0.12	0.13	Muscle	44	0.07/0.03	-0.23
Adrenal	41	0.25/0.12	-0.38[d]	Urine	8	0.06/0.11	0.24
Blood	43	0.21/0.09	-0.29	Adipose	43	0.04/0.01	0.11
Prostate	41	0.20/0.22	-0.08				

[a] Source: Gross, et al. Reprinted with permission from Toxicology and Applied Pharmacology. (c) Academic Press, Inc., 1975.

[b] Shown are number of tissues (N), their means ±SD and correlation of tissue concentrations vs age.

[c] $p < 0.01$.

[d] $p < 0.05$.

Table 6.5 CONCENTRATIONS OF LEAD FOR TISSUES INCREASING WITH AGE[a,b]
ppm, wet-weight basis

Tissue	Decade, years					
	20–29	30–39	40–49	50–59	60–69	70–79
Tibia	6.61±0.92 (6)	9.37±4.64 (4)	10.77±5.09 (8)	9.68±4.43 (9)	18.57±8.34 (11)	28.36±21.37 (6)
Skull	7.27±1.76 (6)	9.07±4.31 (4)	12.85±5.12 (8)	10.13±4.21 (9)	19.60±8.17 (11)	21.76±18.06 (5)
Rib	4.06±1.92 (6)	5.48±3.82 (4)	8.04±4.13 (8)	4.83±1.55 (9)	9.77±4.36 (11)	9.42±4.65 (6)
Vertebrae	3.48±1.50 (6)	2.98±1.84 (4)	4.98±1.52 (8)	2.88±1.20 (9)	6.66±3.24 (11)	4.17±2.26 (6)
Aorta	0.40±0.18 (6)	0.86±0.71 (4)	0.75±0.16 (8)	1.14±0.46 (9)	2.83±2.55 (11)	3.32±2.18 (6)

[a] Source: Gross, et al. Reprinted with permission from Toxicology and Applied Pharmacology. (c) Academic Press. Inc. 1975.

[b] Shown are the decade means ±SD. The number of tissues in each decade are shown in parentheses.

was found. The median lead concentration in the cerebrum and cerebellum was 0.19 and 0.22 ppm, respectively.

Lead is normally found in higher concentrations (on a weight per weight basis) in hair than in any tissue. Kopito, et al., (1967), in a study of 93 presumably healthy children under 17 years of age from the greater Boston area, found a mean lead concentration of 31 micrograms per gram of hair.

Several studies have shown that lead concentrations in hair and teeth vary among groups of individuals, depending on the amount of lead in their immediate environments. These are discussed in Section 6.5.2.

6.2.3 Elimination

The principal routes of elimination of lead from the body are through the feces and urine. Secondary routes include sweat, milk, falling hair, and discarded and desquamated skin. Kehoe has suggested that the contribution of food, beverages and water digested and of the total urine and feces excreted can be used to determine the net balance of lead intake versus output over a period of many months (Kehoe, 1961- a-d; see Table 6.6)

Kehoe's work indicates that in conditions approximating a steady-state in which oral input roughly parallels urinary and fecal output, the urinary excretion is about 10 percent of the oral output and the fecal output is close to 90 percent. Most of the lead in the feces represents lead which has passed unabsorbed through the gut. The contribution to total excretion of inhaled lead was not determined, a factor which would have likely elevated the estimated proportion of the total lead intake excreted via the urine.

Several investigations have indicated that lead excreted (rather than that passing unabsorbed through the intestine) in the feces derives predominantly from the bile. For example, Blaxter and Cowie (1946) found that 7.5 percent of a dose of lead acetate administered to sheep was excreted in 6 days. Eighty-one percent of that was in the bile.

After intraveneous administration of lead-212, the fecal route probably contributes as much as the urinary route to total excretion. In a study on two human subjects, Booker, et al., (1969), found no lead-212 in the feces during the first 24 hours after injection but found 4.4 and 5.6 percent in the urine. During the second 24 hours, however, they found 1.4 percent in the urine and 1.5 percent in the feces.

The excretion of lead through the kidney is hampered by the high degree of interaction of lead and other heavy metals with ligands present in erythrocytes and/or plasma proteins. Vostal and Heller (1968) investigated lead excretion in man and dogs and found that the renal tubule reabsorbed a constant amount of lead. The effect was pH-dependent, increased at low pH and decreased or was entirely absent at high pH.

Rabinowitz, et al., (1973), studied lead excretion as part of a study of the kinetics of lead metabolism using stable lead isotope (^{204}Pb and ^{207}Pb)

Table 6.6 LEAD INGESTION AND EXCRETION OF A NORMAL HUMAN SUBJECT[a]

8-Week Periods	Lead Ingested, mg	Lead Excreted, mg			Net Change in Body Lead, mg
		Total	In Feces	In Urine	
1st	13.59	11.95	10.45	1.50	+1.64
2nd	13.31	15.13	13.63	1.50	-1.82
3rd	13.16	13.82	12.45	1.37	-0.66
4th	11.51	11.59	10.41	1.18	-0.08
5th	9.30	8.93	7.88	1.05	+0.37
6th	9.24	9.05	8.16	0.89	+0.19
7th	12.75	13.74	12.86	0.88	-0.99
Subtotal	82.86	84.21	75.84	8.37	-1.35
8th	22.21	17.61	15.85	1.76	+4.60
9th	18.17	15.05	13.76	1.29	+3.12
Subtotal	40.38	32.66	29.61	3.05	+7.72
Total	123.24	116.87	105.45	11.42	+6.37

[a] Source: Kehoe (1961a-d). Reprinted from Journal Royal Institute Public Health Hygiene.

tracers. A normal, healthy man ate a constant, low-lead diet (156 micrograms lead per day for 160 days while living in a metabolic unit. It was found that 8.3 plus or minus 0.4 percent of the ingested ^{204}Pb was absorbed into the blood, where it had a mean life of 27 days. Fifty-four percent of this lead was lost from blood through the urine, which had an isotopic composition identical with whole blood; the remainder was transferred to the soft tissues and skeleton. The net absorption of lead was 25 micrograms per day with a mean urinary excretion of 28 micrograms per day. Loss of lead from hair, nails, and sweat was approximately 4 micrograms per day. Therefore the total lead output exceeded dietary intake by 17 micrograms per day, which presumably came from the atmosphere. This value agreed generally with that derived from the analysis of isotopic blood data.

The estimates of half-time for lead in bone have varied from 64 days in the spine of rats (Torvik, et al., 1974) to 7,500 days in the skeleton of a dog (Fisher, 1969). The half-time varies with different bones, presumably due to the relative proportions of cortical and trabecular bone. The International Commission on Radiological Protection (ICRP) has used 10 years as the biological half-life for lead in bones of humans (ICRP, 1959). Following a single dose of ^{210}Pb in dogs, disappearance of the label from blood was followed for 280 days. The biological half-life of lead in the body was estimated to be 1940 days (Hursh, 1973).

Prerovska and Teisinger (1970), in a study of the excretion of lead and its biological activity several years after termination of exposure, concluded that there are at least two compartments for lead in bone. Hammond, et al., (1967) also suggested an additional compartment consisting of lead firmly bound to soft tissue. This conclusion is consistent with the observation by Goyer and Mahaffey (1972) and Moore and Goyer (1974) who found that lead binds firmly with nuclear protein in rats. Studies in animals by Bolanowska, et al., (1968) and Bolanowska and Piotrowski (1968, 1969) have furnished mathematical models for the elimination of lead based upon an exponential model for a four-component system:

(1) A rapid exchange compartment (blood and internal organs);
(2) The skin and muscles;
(3) The exchangeable part of lead in bones; and
(4) A very slowly exchangeable part of lead in bone.

Body retention for bone-seekers is best described by a power function of the form:

$$R_t = At^{-n}$$

where,

R_t = fraction of original dose at time t;
A = a constant equal to the fraction of the assimilated dose at $t = 1$; and
n = a constant equal to the slope of a linear log - log plot of R against t, is a coefficient characterizing the loss from the body.

6.2.4 Mathematical Models of Lead Metabolism

Some researchers have examined the total uptake of lead by humans. This involves multiple routes of entry, each with characteristic absorption patterns.

Rustagi (1964, 1965) and Sterling (1964) propose the use of the log-normal distribution for the random phenomena of the intake and output of trace metals, including lead, in the human system. Some results of the queuing theory in probability are indicated through the use of this mathematical model for the expected amount stored in the body.

Lutz, et al., (1970) developed a mathematical model to represent the environmental transport of lead from several sources, with the subsequent uptake of lead by man. In particular, the submodels for airborne transport of lead and lead in the body were developed. The model developed for the airborne transport of lead was used to calculate the airborne concentrations of lead in the atmosphere due to emissions of lead from several sources. The predicted output is for an average steady-state airborne lead concentration, as the model was not developed to predict time-varying airborne lead concentrations.

The submodel, which represents the flow of lead into, within, and out of an individual was developed to predict the distribution and quantity of lead in several body organs. Since measurement of the blood-lead level of an individual is a clinical method of investigating the effect of lead on an individual, the blood-lead levels due to several modes of intake of lead, including inhalation of various concentrations of airborne lead and ingestion of normal amounts and above normal amounts, were calculated. The approach of developing a mathematical model to quantitatively predict blood-lead levels due to intake by ingestion or inhalation was found to be valid within the accuracy of this preliminary modeling effort.

In order to approximate total lead uptake more accurately it is desirable to first consider each route separately. It should be noted, however, that humans are never limited to a single path of lead entry and studies which do so are abstractions for the purpose of controlled experimentation.

6.3 TOXIC EFFECTS

The present-day environmental problem of lead may be viewed at three levels. First, there is the problem of sporadic episodes of acute lead intoxication. These are largely accidental or the result of ignorance of the danger of lead. Second is the problem of clinical and subclinical intoxication of large numbers of children in urban ghetto areas who are living in pre-World War II housing. This is largely a socioeconomic problem but it is left to members of the medical community to promulgate information regarding the dimensions of the problem. The third aspect of the environmental problem concerns the question of the possible harmful effects of body stores of lead.

An answer to this question depends on increased knowledge of the biologic effects of lead, particularly regarding the effect of trace quantities on cellular function (Goyer, 1971a).

Many organs and systems have been shown to be adversely affected by lead. These effects will be discussed in succeeding sections of this chapter. Much of what is known concerning effects has been adduced only in isolated cellular or subcellular systems. The implications for the health of man are uncertain in such cases but should be further investigated when the level of lead in the study is within an order of magnitude of likely human exposure levels.

6.3.1 Enzymatic and Cellular Responses to Lead

The basic mechanism of chemical toxicities is ultimately associated with the chemical and physical properties of the toxic agent. Metal toxicity is the inherent capacity of the metal to adversely affect any biological activity. This is the result of a metal interacting with an enzyme, an enzyme substrate, or a protein, thereby leading to changes in metabolic or physiologic processes.

Toxicity may also result from interference with essential metal metabolism, and from interactions with macromolecules causing conformational changes and disturbances in cell membrane permeability. Lead exhibits high affinity for most biological anions. For example, the solubility product for lead phosphate is 10^{-30}, making binding between the two ionic species (Pb^{++} and PO_4^{--}) most likely both inside and outside living cells (Venugopal and Luckey, 1975).

Although the enzymes affected by lead mainly are involved in heme synthesis, activities of other enzymes are also influenced by lead. These activities may be manifested in two general ways: (1) increased enzyme activity in the blood plasma due to tissue damage, or (2) decreased enzyme activity due to an inhibitory action on certain enzymes in tissues or in the blood (de Bruin, 1971).

Ulmer and Vallee (1969) and Vallee and Ulmer (1972) have reported the effects of lead on diverse biological systems ranging in complexity from isolated biochemical systems to whole animals. Vallee and Ulmer (1972) indicate that lead, like mercury and cadmium, forms mercaptides with the -SH group of cysteine and less stable complexes with other amino acid side chains. This apparently is inhibitory to a number of enzymes.

The stability constants of complexes of Pb^{++} with serine and threonine are equivalent to those with Zn^{++} and greater than those with Cu^{++}, Ni^{++}, Co^{++}, and Mn^{++}. Proteins with large numbers of free -SH groupgs, e.g., thionein bind Pb^{++} firmly both *in vitro* and *in vivo*.

Lead inhibits most enzymes bearing a single functional -SH group less readily than either Hg^{++} or Cd^{++}. The concentrations of Pb^{++} generally required to inhibit -SH and other enzymes *in vitro*, i.e., 10^{-3} to 10^{-4} M, is far in excess of those levels observed in tissues and fluids from individuals with clinically evident Pb intoxication. However, much lower concentrations of Pb^{++} inhibit a small, select group of enzymes, i.e., lipoamide dehydrogenase, certain ATPases, and deltaaminolevulinic acid (ALAD) dehydrase (Vallee and Ulmer, 1972). In fact, Ulmer and Vallee (1969) found that lead (as Pb^{++}) in concentrations as low as 6.5×10^{-6} M strongly inhibits lipoamide dehydrogenase, an enzyme crucial to cellular oxidation. This probably occurs through binding to the dithiol configuration at the active catalytic center. Protection is afforded by coenzymes and substrates and the inhibition is reversed by EDTA.

Increased activity of the transaminases (serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase) have been described by some investigators while such effects have not been observed by others. Animal studies of enzyme enhancement and depression were reviewed by Vallee and Ulmer (1972) and are summarized in Tables 6.7 and 6.8.

There is some indication that lead absorption by man may increase the activity of aldolase and catalase while depressing the activity of alkaline phosphatase, cholinesterase, and carbonic anhydrase. These effects were reviewed by de Bruin (1971). Workers with moderate elevations of blood lead have been found to have red blood cells with reduced adenosine hyphosphatase activity (Hasan, et al., 1967a,b). The clinical implications of this enzyme alteration are unknown, although it is quite possibly a factor in the shortened erythrocyte life span which occurs upon exposure to high levels of lead.

In a study of the detoxication mechanism in the rat, Wagstaff (1972) observed that ingestion of lead acetate was followed by increased activity of microsomal enzymes. No rats died due to lead acetate consumption but body weight gains were depressed. Male rats fed lead acetate had elevated cytochrome P-450.

The effect of lead acetate on phenobarbital, a microsomal enzyme stimulant, was additive or even synergistic in liver weight increases, hexobarbital sleep time, and *in vitro* enzyme activities. Concurrent ingestion of phenobarbital with lead decreased toxicity. The physical appearance of lead-fed rats was improved, impairment of body weight gain was practically eliminated, and storage of lead in liver tissue was decreased 39 percent by phenobarbital.

Contrary to these findings, rates of P-450 mediated drug metabolism in adults and children appear to be prolonged in some cases of high exposure (Alvares, et al., 1975; Alvares, et al., 1976). Furthermore, even in rats, contradictory observations have been made indicating depression of P-450 dependent drug metabolism (Scoppa, et al., 1973).

Nathanson and Bloom (1975) found that very low concentrations of lead nitrate inhibit adenyl cyclase in mammalian (rat) brain tissue. In cerebellar homogenates, enzyme activity was inhibited by concentrations of lead nitrate or lead chloride as low as 0.1 micromolar; 50 percent inhibition occurred at about 3 micromolar; and almost complete inhibition occurred at

Table 6.7 ENZYMATIC ACTIVITIES ENHANCED BY LEAD[a]

Enzyme	Source
Alkaline phosphatase	Guinea pig urine
Cytochrome oxidase	Canine intestine
Glucose-6-P dehydrogenase	Guinea pig kidney
Glutamic dehydrogenase	Guinea pig serum and urine
Glutamic oxaloacetic transaminase	Sheep red cells; guinea pig serum
Glutamic pyruvate transaminase	Sheep plasma and red cells
Lactic dehydrogenase	Guinea pig serum and kidney
Sorbital dehydrogenase	Guinea pig serum
Steroid 3 β-ol-dehydrogenase	Rabbit adrenal

[a] Source: Vallee and Ulmer. Reprinted with permission from Annual Reviews Biochemistry. (c) Annual Reviews, Inc., 1972.

Table 6.8 ENZYMATIC ACTIVITIES INHIBITED BY LEAD[a]

Enzyme	Source
Acetylcholinesterase	Rat red cells Equine serum Sheep brain
Acid phosphatase	Rabbit liver and kidney
Alkaline phosphatase	Rabbit and human serum Rabbit muscle, intestine Rabbit blood vessels Rat lung
δ-ALA dehydrase	Mammamlian red cells
Aminopeptidase	Cat and guinea pig liver
ATPases	Rabbit muscle, blood vessels Human red cells Guinea pig kidney
Carbonic anhydrase	Human blood
Cytochrome oxidase	Canine intestine
Diaphorase	Rabbit muscle
Fructose-1,6-diphosphatase	*C. utilis*
Glucose-6-P dehydrogenase	Rat red cells Human red cells
Glutamic dehydrogenase	Guinea pig kidney
Succinic dehydrogenase	Canine intestine

[a] Source: Vallee and Ulmer. Reprinted with permission from Annual Reviews Biochemistry. (c) Annual Reviews, Inc. 1972.

100 micromolar. Lead ions also inhibited noradrenaline-stimulated activity, independent of the concentration of adenosine triphosphate (ATP) and tissue protein present in the reaction mixture. In cases of experimental lead intoxication in which rats displayed symptoms of hyperactivity, brain lead levels varied from 3.0 to 6.0 micromoles, a concentration in which adenyl cyclase activity was inhibited by 50 to 70 percent. These animal studies of Nathanson and Bloom (1975) support the suggestion that inhibition of adenyl cyclase may mediate some of the toxic manifestations of lead in the nervous system and other organ systems in man.

Phillips, et al., (1971) investigated the effects of lead ingestion on the body burden of DDT, liver Vitamin A and microsomal enzyme activity in the rat. Lead ingestion at 100 to 200 ppm (as lead acetate) for 36 and 90 days had no effect on the disappearance of DDT residues (and metabolites) from adipose tissue of rats. Lead alone and lead fed to DDT pretreated animals had no effect on body weight gain, liver weights, liver Vitamin A, liver protein, *in vitro* liver carboxylesterase activity and phenobarbital sleeping times.

Suketa, et al., (1975) found that the amount of delta-aminolevulinic acid (ALA) increased four times in lead-intoxicated rats compared with controls. The formation of ALA in the liver homogenate of lead-intoxicated rats was increased by the addition of ethylenediamine-tetraacetic acid (EDTA), suggesting that the increase of ALA in the liver of lead-intoxicated rats may be due to the activation of ALA synthetase by lead rather than due to the inhibition of ALA dehydratase by lead. While the full physiological consequences of the lead inhibition of enzymes are not generally understood, research has focused on enzymes of the hematological system (see Section 6.3.2.2).

Within cells, lead has the greatest affinity for mitochondrial membranes and nuclei (Goyer and Moore, 1974). Lead forms complexes with the phosphate groups of nucleotides and nucleic acids and catalyzes a nonenzymatic hydrolysis of nucleosidetriphosphates (particularly ATP). Lead also hydrolyzes RNA in other systems, and brief exposure of phenylalanyl and lysyl tRNA to Pb^{++} inhibits their binding to ribosomes as reviewed by Vallee and Ulmer (1972).

Nuclear lead binds with an acidic protein fraction and accumulates to form a discrete inclusion body which has a characteristic ultrastructure (Goyer and Moore, 1974). A common occurrence in humans and animals who suffer from lead intoxication is the presence of discrete, densely-staining intranuclear inclusion bodies within hepatic parenchymal cells and renal tubular cells. When the renal tubular cell is presented with large concentrations of lead, intracytoplasmic concretions are formed. The relationship of these concretions to the lysosomal system has not been demonstrated but dense staining bodies do form in secondary lysosomes derived from degenerating lead-intoxicated mitochondria (Goyer and Moore, 1974).

Two forms of lead-containing, intranuclear inclusion bodies isolated from kidney tubule cells of chronically lead-poisoned rats seem also to be present in rabbits and man. Goyer (1971a) proposed that these inclusion bodies act as a protective mechanism by converting toxic lead into a non-diffusible form, thus diminishing its effects on mitochondria and other physiological receptors (see Figure 6.9). Inclusion bodies appear in acid-fast-stained smears of the urinary sediment of children, which may provide a technique for assessing kidney toxicity following lead exposure (Landing and Nakai, 1959). The subcellular distribution of lead in the kidney following the feeding of lead to rats for 4 months is shown in Figure 6.10. These data show that the largest increase in lead content is in the nucleus where most is bound to an inclusion body (see Section 6.3.2.1).

The high affinity of mitochondria for lead results in morphological and functional alterations. Alteration of mitochondrial structure or cellular oxidation processes, or both, has been verified in canine intestine, rabbit liver, human placenta, rat liver, rat kidney, and corn mitochondria (see Section 6.3.1). In many instances, inhibition is reversed by EDTA according to Vallee and Ulmer (1972). These authors also report that lead ions (Pb^{++}) bind to insoluble ferric hydroxide and to ferritin in vitro, which suggests that iron storage is altered in this condition.

Mitochondrial swelling has been demonstrated in renal tubular cells of lead-poisoned humans and animals (Goyer, 1971a). Experimentally lead-poisoned animals possess mitochondria with impaired respiratory and phosphorylative abilities. The effects of lead on mitochondria appear to result from: (1) inhibition of certain enzymes such as succinic dehydrogenase; (2) activation of energy-dependent ion movement and the resulting increased respiration supporting these movements; (3) energy-dependent movement of lead itself; and (4) effects of lead on substrate uptake and retention (Scott, et al., 1971). Walton (1973) suggests that the effects of lead on the mitochondria are two-fold; (1) prevention of ATP synthesis and interference with the maintenance of ionic concentration gradients across the membrane; and (2) hydrolysis of ATP, formation of complexes with the thiol groups of mitochondrial enzymes such as those involved in cytochrome synthesis, and reaction with ions such as phosphates.

In a study on the cytotoxicity of lead, Beck, et al., (1973) report that lead oxide and airborne dust have a toxic effect on line L cells as manifested by division inhibition and disturbance of cell permeability and intermediary metabolism. The reproduction of connective tissue cells in the human fetus is also impaired. Bullate vacuolation is caused both by lead oxide and airborne dust and is comparable in alveolar macrophages, line L cells, and connective tissue cells in the human fetus.

6.3.2 Organ System Toxicities

6.3.2.1 Renal Toxicity--

A large body of evidence implicates lead as a causative agent in kidney disease. Goyer and Rhyne's (1973) review of the pathological effects of lead indicates that in humans suffering from acute lead toxicity (encephalopathy, lead-induced anemia), the kidney exhibits nonspecific degenerative changes in the tubular lining. The proximal tubular cells are the most seriously

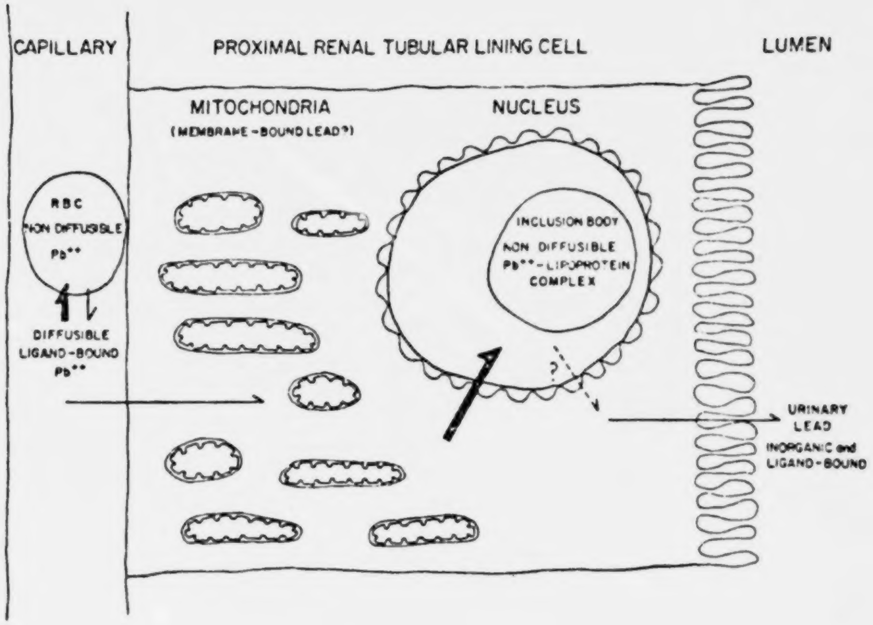
CAPILLARY
PROXIMAL RENAL TUBULAR LINING CELL
LUMEN
MITOCHONDRIA
(MEMBRANE-BOUND LEAD?)
NUCLEUS
RBC
NON DIFFUSIBLE
Pb++
DIFFUSIBLE
LIGAND-BOUND
Pb++
INCLUSION BODY
NON DIFFUSIBLE
Pb++-LIPOPROTEIN
COMPLEX
?
URINARY
LEAD
INORGANIC and
LIGAND-BOUND

Figure 6.9 Scheme showing role of intranuclear inclusion body in the metabolism of lead. Source: Goyer. Reprinted with permission from Laboratory Investigations. (c) International Academy of Pathology, 1971.

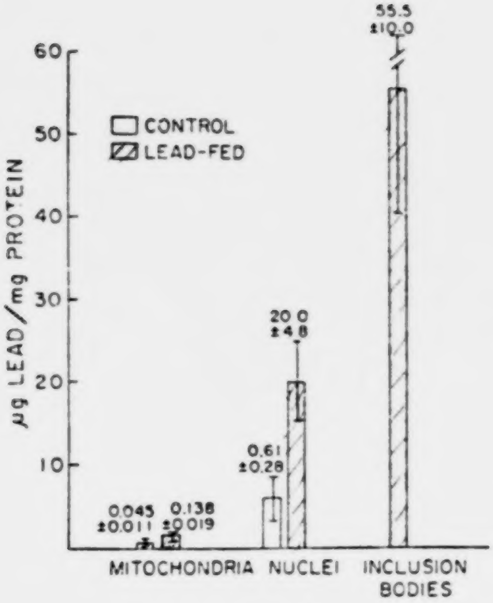

Figure 6.10 Lead content of subcellular fractions from kidneys of control and lead-fed rats. Source: Goyer. Reprinted with permission from Laboratory Investigations. (c) International Academy of Pathology, 1971.

affected, manifesting inclusion bodies within their nuclei. In many instances, hyperaminoacidemia is seen when blood levels are greater than 80 micrograms lead per 100 milliliters (Chisolm, 1962). This toxicity seems to be completely reversible in many instances.

Renal tubular dysfunction in lead toxicity is thought to arise from the effects of lead on mitochondrial function. This has great significance in terms of toxicity becuase of the high affinity of mitochondria for lead (see Section 6.3.1).

Mitochondrial accumulation of lead in kidneys is potentially damaging for normal renal function, as ADP-stimulated respiration in mitochondria is completely inhibited on incubation with lead. Mitochondria from the proximal convoluted tubules of lead-loaded rats generally show a reduced rate of respiration and partial uncoupling of oxidative phosphorylation, perhaps as a consequence of altered outer membrane structure. This impairment of energy metabolism may be responsible for the reduced transport function of the kidney and therefore the occurrence of aminoaciduria and glycosuria in lead toxicity. The respiratory abnormalities in renal mitochondria may result from their reduced cytochrome content. (Rhyne and Goyer, 1971).

Renal cells, though functionally impaired, are still viable, even at cellular lead concentrations which are lethal to mitochondria in *in vitro* studies. This suggests some protective mechanism operating within the renal cell to limit mitochondrial uptake of lead, which may be the role of renal intranuclear inclusion bodies. As concentrations of lead in renal tubular lining cells increase, much of the additional metal is found in the nuclear fraction, with over 50 percent of this in the form of inclusion bodies. Renal lead is thus maintained in a nondiffusible, nontoxic form until the cell in which the inclusion body exists is itself excreted in the urine. In this way the kidney can excrete large amounts of lead without excessive damage to the tubular lining cells (see Section 6.3.1).

At blood-lead concentrations of 150 micrograms per 100 milliters or more, the Fanconi triad (hyperaminoaciduria, glycosuria, and hypophosphatemia accompanied by hyperphosphaturia) is seen in approximately one-third of the patients wich acute lead encephalopathy (Leaf, 1966). This indicates some degree of tubular damage. The aminoaciduria is related to the severity of clinical toxicity, and disappears following chelation therapy and cessation of lead intake.

The association between chronic lead exposure and nephropathy has been controversial. Hamilton and Hardy (1974) reviewed studies made 40 or more years ago which indicated a positive association. One report suggested that industrial lead workers had three times the incidence of kidney damage as compared to the controls. In Queensland, Australia, a high incidence of deaths from chronic nephritis was reported in persons who had experienced, when children, acute plumbism from the ingestion of leaded paint. Subsequently, many of these same people in Queensland developed renal gout (Emmerson, 1968). Women were overrepresented among these lead gout patients compared to patients with idiopathic gout. Also, lead gout patients have normal triglyceride and cholesterol levels but those with idiopathic gout develop hypertriglyceridemia (Emmerson and Knowleds, 1971).

Studies in the U. S. have not confirmed these results. Tepper (1963) found no evidence for chronic renal disease in persons who had confirmed lead intoxication as children 10 to 30 years previously. He suggested that the Queensland children were exposed to lead over a more protracted period of time than the American children. In contrast to the Australian people, the American subjects exhibited no excess in lead body burden as demonstrated by the administration of EDTA.

Goyer and Rhyne (1973) cited reports which suggested that prolonged industrial lead exposure induced chronic nephropathy and renal failure in countries where occupational exposure to lead was not closely controlled. Studies with Japanese lead workers indicated that 10 workers excreted lead in the urine, ranging in concentration from 168 to 603 micrograms lead per liter, whereas controls (office workers) excreted 12 to 98 micrograms per liter (Goyer, et al., 1972). In the lead group significant elevations were also seen for alpha-amino nitrogen excretion, urinary delta-aminolevulinic acid and urinary coproporphyrins, but only one of the 10 workers exhibited hyperaminoaciduria. Similarly, Cramer, et al., (1974) found no excess aminoaciduria in lead workers whose exposure varied from 4 to 20 years. Kidney biopsies in five of the seven workers demonstrated mitochondrial changes and ultrastructural changes in the proximal tubules of all five men, and lead inclusions were found in the nuclei of two. Renal function tests were normal in all except one worker who had a reduced glomerular filtration rate.

The existence of lead nephropathy resulting from occupational exposure to lead appears to be well substantiated in American lead workers. Among eight subjects suspected of excessive occupational exposure to lead, detailed examination of renal function identified abnormalities in four (Wedeen, et al., 1975). The glomerular filtration rate was less than 87 milliliters per minute per 1.73 square meters in one subject with asymptomatic renal failure and in three subjects with preclinical renal dysfunction. A survey of death certificates from 7,032 battery and smelting workers (Cooper and Gaffey, 1975) revealed a "consistent excess of deaths from 'other hypertensive' and 'chronic nephritis or other renal sclerosis'". These and other findings suggest that occupational lead nephropathy may indeed represent a significant health hazard in the United States lead industry and is by no means unusual among lead workers.

Many of the signs that appear in humans suspected of suffering from lead toxicity also occur in experimental animals which are fed lead. These include hyperaminoacidemia, intranuclear inclusion bodies, proximal tubular damage, and hyperuricemia (Goyer and Rhyne, 1973). These authors concluded that "chronic" effects of lead on the kidney are dependent on a particular renal content of lead over a prolonged period of time, and that lead is certainly capable of inducing a chronic nephropathy. Figure 6.11 depicts a scheme which relates lead concentrations of drinking water to kidney lead content and various pathological conditions which appear in rats after 10

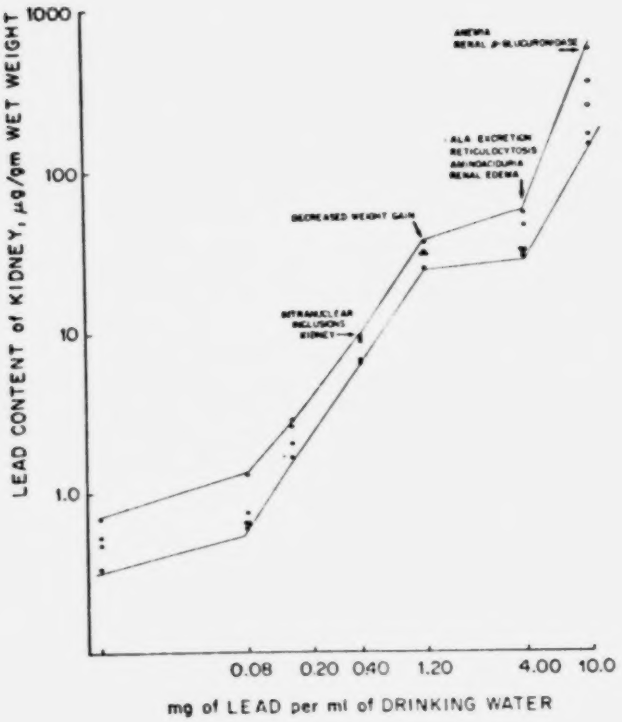

Figure 6.11 Correlation of lead content of kidney and different doses of lead fed to rats for 10 weeks with various parameters of lead toxicity. Source: Goyer and Ryne. Reprinted with permission from International Review Experimental Pathology, (c) Academic Press, Inc. 1973.

weeks of exposure to lead. Schroeder (1973) also noticed that 250 micrograms of lead (as lead acetate) per 100 milliliters given to rats in drinking water since weaning caused substantial increases in glycosuria and proteinuria. The former study perhaps relates more closely to the lead exposure of industrial workers who often are found to have intranuclear inclusion bodies, whereas the latter is a closer approximation to other groups not exposed to the high lead environment.

Choie and Richter (1972) found that a single dose of lead (0.05 milligram per gram of body weight) as lead acetate induced characteristic intranuclear inclusions in the epithelium of proximal tubules in rat kidneys within 1 to 6 days. The development of the intranuclear inclusions is thus an acute manifestation of lead poisoning, not a delayed one, as has been thought hitherto.

Goyer (1971b) reported that rats tolerate long-term feeding of a diet containing one percent lead as lead acetate, with the kidneys undergoing a series of pathological changes. These changes commence with proximal tubular dysfunction and progress to cellular hyperplasia, medullary cysts and interstitial fibrosis. Renal adenocarcinoma develops in a large percentage of the rats (see Section 6.3.5). There is no evidence, however, that lead poisoning or chronic, subclinical lead intoxication in man is related to cancer in the kidney or any other organ of man.

The endocrine function of the kidney following lead intake has been partially evaluated. Sandstead, et al., (1970) noted that nine men with confirmed subclinical lead intoxication failed to respond to a low sodium diet in the normal manner. The subjects' plasma renin activity and aldosterone secretion rate did not reach the normal range. Lead induces a marked inhibition of Na^+/K^+ ATPase from renal homogenates of lead-poisoned animals which interferes with tubular Na^+ absorption. This indicates that lead acts as an antagonist to sodium conservation by the kidney.

6.3.2.2 Hematopoietic Toxicity--

De Bruin (1971) identified three different aspects of the effects of lead on hematopoiesis:

(1) The influence of lead on circulating erythrocytes;
(2) The impairment of the production of hemoglobin resulting from the effects of lead upon the bone marrow; and
(3) The stimulation of erythropoiesis in the bone marrow.

In relation to these effects the following biochemical events can be observed:

(1) In urine:

Porphyrinuria: increased excretory output of coproporphyrin 3. Elevated excretion of delta-aminolevulinic acid (5-aminolevulinic acid [ALAD]). Slight rise of urinary level of porphobilinogen.

(2) In blood:

a. In serum: Increased content of ALA.

b. In mature erythrocytes in peripheral blood: Elevated concentration of protoporphyrin 9 and the coproporphyrins.
Increase in concentration of iron unattached to hemoglobin
Decrease in hemoglobin level
Reduction in numbers of erythrocytes
Decrease in aminolevulinic acid dehydratase (ALAD)
Occurrence of punctate basophilia
Occurrence of siderocytes
Occurrence of reticulocytosis
Increase in their osmotic resistance
Enhancement of their outflow of potassium
Shortening of their survival

(3) In the bone marrow cells:

Occurrence of morphological changes, i.e., basophilia, siderocytes, increased numbers of erythroblasts and, sometimes, of megaloblasts and macroblasts
Degenerative alterations of mitochondria in association with presence of ferritin molecules

(4) In tissue cells:

Accumulation of porphyrins in liver, kidney, and in cells of bone marrow in some species of experimentally poisoned animals.

Albahary (1972) further described several effects of chronic inorganic lead poisoning on the bone marrow and peripheral blood. For example, the mitochondria and the ribosomes of the erythroblasts and the reticulocytes are known to be damaged, leading to the formation of basophilic stippled cells when stained by basic dyes and to abnormalities of heme synthesis. These phenomena, to which the effect of lead in some other tissues (liver, kidney) may be added, cause secondary porphyria, imperfect utilization of iron, and perhaps a minimal globinopathy similar to that in thalassemia minor. Lead inhibits medullary erythropoiesis and increases the fragility of red cell membranes which shortens their life span.

Anemia is often seen as a manifestation of acute or chronic lead poisoning and may be the only clinical sign of chronic exposure to low levels of lead (Goyer and Rhyne, 1973). It appears to be the combined result of impaired heme synthesis and the hemolytic action of lead. The integrity of red cell membranes and globin play a role in the anemia of lead poisoning. Stippling of red blood cells is often seen in lead-induced anemia along with microcytic and hypochromic cells. Stippled cells are more prevalent among immature red cells in the marrow than in peripheral blood (Waldron, 1966). The appearance of granules in red blood cells was used as an indication of lead intoxication in the past, but this is a very nonspecific test.

Altered osmotic and mechanical fragility of erythrocytes may be due to lead impairment of glycolytic enzyme activity (Goyer and Rhyne, 1973), although experimental support is lacking. Damage of the red blood cell by the liberation of free acids, subsequent to the (1) formation of a lead-inorganic phosphate complex with red cells or plasma; (2) formation of lead diglycerol sulfate; and (3) coagulation and flocculation of a peptide lead phosphate sol on the cell membrane have all been proposed (Vallee and Ulmer, 1972).

On incubation _in vitro_, lead causes human and rabbit erythrocytes to leak K$^+$ whereas controls take up K$^+$. A corresponding decrease in the activity of erythrocytic membrane Na$^+$/K$^+$-dependent adenosine triphosphatase (ATPase) along with an increase in cellular adenosine triphosphate (ATP) may underlie the K$^+$ loss. A second dose of lead to recovered cells does not increase K$^+$ permeability; this will occur, however, if chelation "therapy" is used (Hasan, et al., 1967b; Passow, et al., 1961). Red blood cells taken from men occupationally exposed to lead exhibited the behavior described above (Hasan, et al., 1967a). The membrane ATPase levels return to normal when exposure to lead ceases or EDTA therapy has been started.

The effect on the membrane is an early response to lead and appears long before clinical symptoms are obvious. There is also an effect on the uptake of ^{32}P by red blood cells which is reduced in men having severe exposure to lead.

According to de Kretser and Waldron (1963), Aub, et al., (1926) observed that leaded red cells were less resistant to mechanical trauma than normal cells, an observation which has also been reported by some other workers. Other research, however, has shown the mechanical fragility to be normal in lead poisoning. De Kretser and Waldron (1963) found that there was no increase in the mechanical fragility of cells leaded _in vitro_ until the concentration of lead was greater than 10 micrograms per milliliter, and that at a concentration of 45 micrograms Pb^{++} per milliliter, saturation was reached. It should be noted that these concentrations are greatly in excess of the usual _in vivo_ solutions.

Red cell survival is shortened in lead poisoning. Using tritiated diisopropyl fluorophosphate as a tracer for red blood cells, Hernberg, et al., (1967) showed that the red cell half-life was shortened in humans occupationally exposed to lead. The half-life decreased to less than 105 days at blood lead concentrations of 80 micrograms per 100 grams of whole blood. In acute lead poisoning, hemolysis is the predominant factor. decreasing the life span of red cells.

In normal red cell precursors, the synthesis of heme and globin is finely balanced but in diseases such as sideroblastic anemia and iron-deficiency anemia, a defect in heme synthesis leads to a disturbance of globin synthesis. Defective globin synthesis occurs in lead poisoning according to White and Harvey (1972) who indicate that the abnormal synthesis of alpha and beta globin chains plays a role in the pathogenesis of lead poisoning anemia. When heme-deficient reticulocytes are incubated with lead in vitro, polysomal disaggregation occurs. This supports an alternative explanation that the disordered globin synthesis in lead poisoning is due in part to heme deficiency.

A detailed examination of the steps in the synthesis of heme (see Figures 6.12 and 6.13) indicates that lead can to some extent affect steps of heme synthesis, although the degree of inhibition and the concentration of the required elements vary considerably. Lead interference in heme synthesis is reflected in the high levels of excreted porphyrin precursors in the urine (Milic, et al., 1973).

The most lead-sensitive enzymes are: (1) ALA dehydratase (ALAD) which converts delta-aminolevulinic acid to porphobilinogen; and (2) ferrochelatase which aids the incorporation of iron into protoporphrinogen thereby forming hemes. Inhibition both at these sites, and in the conversion of coproporphyrinogen to protoporphyrinogen is indicated in experimental lead toxicity in animals and in lead poisoning in man by the accumulation and excretion of porphyrins and their precursors.

A decreased activity of ALAD in mature erythrocytes is considered to be a very early biological sign of exposure to lead. ALAD appears, in vivo and in vitro, to be extremely sensitive to the effect of inorganic lead. ALAD activity becomes inhibited even during the very first days of new lead exposure, and its activity is closely and inversely correlated with the concentration of lead in blood even within the "normal blood-lead range", i.e., 0.7 to 1.9 micromoles per liter (15 to 40 micrograms per 100 milliliters). Recent studies have shown that erythrocyte ALAD is inhibited to some degree at far lower blood-lead (PbB) concentrations. Although Hernberg, et al., (1970) suggested there is no threshold for this effect, more recent research (Tola, et al., 1973; Granick, et al., 1973) suggests there is a threshold for ALAD inhibition of 10-20 micrograms per 100 milliliters in adults and about 15 micrograms per 100 milliliters in children.

Hernberg (1973) believes that it is possible that the inhibition measured in vitro merely represents a reduction of "reserve enzyme capacity" that is not essential. However, the ALAD test provides, at the very least, a sensitive method for registering biological effects of low lead doses.

Lauwerys, et al., (1973) compared the effect of inorganic lead and cadmium on blood ALAD in 77 workers occupationally exposed to cadmium, and in 73 control workers. The substantial negative correlation found between log ALAD and PbB (r = -0.660) or PbU (urine lead) (r = -0.501) confirmed the existence of an inverse relationship between ALAD activity in red blood cells and PbB even within the "normal" PbB range of 10 to 40 micrograms per 100 milliliters. The potential effect of cadmium on ALAD in the general population should be considered negligible compared to the effect of lead, since ALAD activity and CdB were not correlated. Previous studies by the senior investigator indicate that among three heavy metals - mercury, lead,

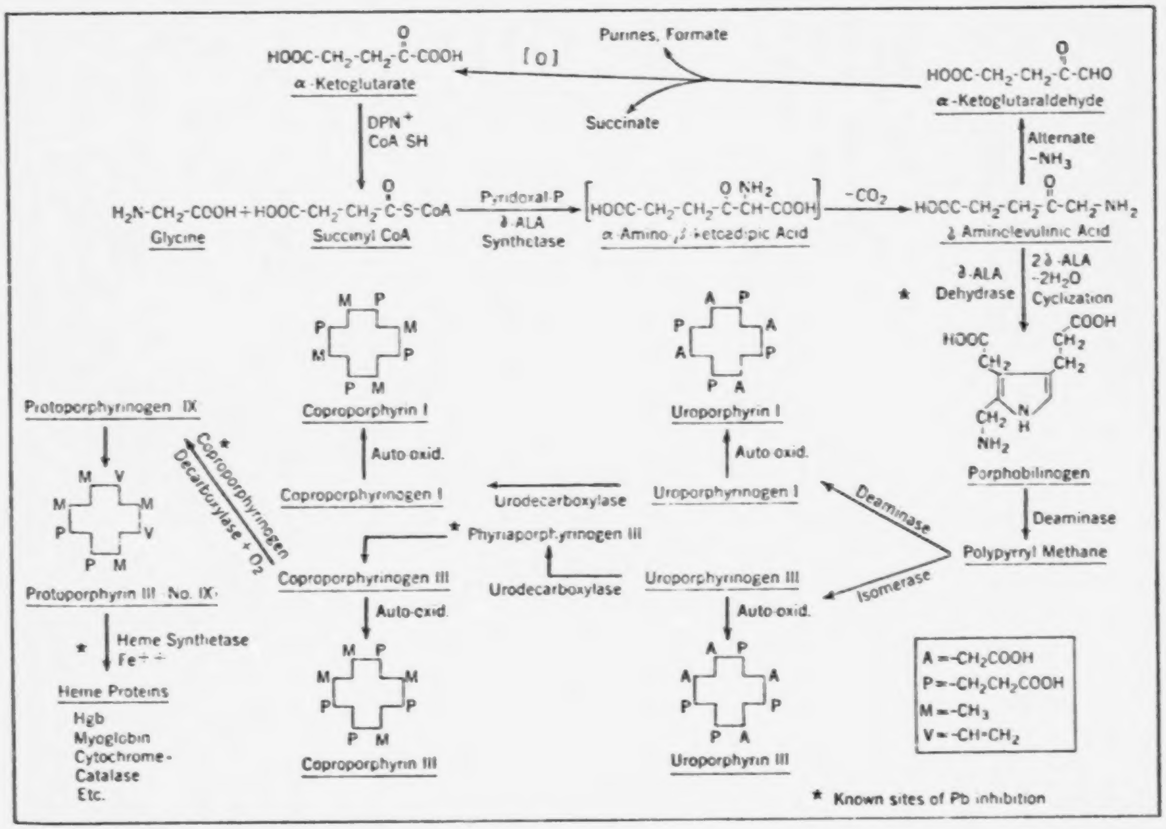
HOOC-CH2-CH2-C(=O)-COOH
α-Ketoglutarate
[O]
Purines, Formate
Succinate
HOOC-CH2-CH2-C(=O)-CHO
α-Ketoglutaraldehyde
DPN+
CoA SH
Alternate
-NH3
H2N-CH2-COOH + HOOC-CH2-CH2-C(=O)-S-CoA
Glycine
Succinyl CoA
Pyridoxal-P
δ-ALA
Synthetase
[HOOC-CH2-CH2-C(=O)-CH(NH2)-COOH]
α-Amino-β-ketoadipic Acid
-CO2
HOOC-CH2-CH2-C(=O)-CH2-NH2
δ Aminolevulinic Acid
δ-ALA
Dehydrase
2 δ-ALA
-2H2O
Cyclization
HOOC
CH2
COOH
CH2
CH2
CH2
NH2
N
H
Porphobilinogen
Deaminase
Polypyrryl Methane
Deaminase
Isomerase
Uroporphyrinogen I
Auto-oxid.
Uroporphyrin I
Uroporphyrinogen III
Auto-oxid.
Uroporphyrin III
Urodecarboxylase
Phyriaporphyrinogen III
Urodecarboxylase
Coproporphyrinogen I
Auto-oxid.
Coproporphyrin I
Coproporphyrinogen III
Auto-oxid.
Coproporphyrin III
Coproporphyrinogen
Decarboxylase + O2
Protoporphyrinogen IX
Protoporphyrin III No. IX
Heme Synthetase
Fe++
Heme Proteins
Hgb
Myoglobin
Cytochrome-
Catalase
Etc.
A = -CH2COOH
P = -CH2CH2COOH
M = -CH3
V = -CH=CH2
* Known sites of Pb inhibition

Figure 6.12 Pathway of heme synthesis. Source: Goldsmith. Reprinted with permission from Journal Air Pollution Control Association. (c) Air Pollution Control Association, 1969.

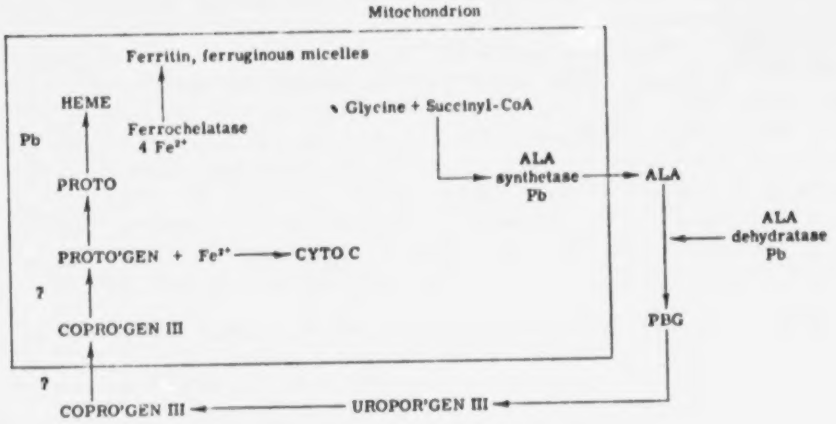
Mitochondrion
Ferritin, ferruginous micelles
HEME
Ferrochelatase
4 Fe^{2+}
Pb
Glycine + Succinyl-CoA
ALA
synthetase
Pb
ALA
PROTO
ALA
dehydratase
Pb
PROTO'GEN + Fe^{2+} → CYTO C
?
COPRO'GEN III
PBG
?
COPRO'GEN III
UROPOR'GEN III

Figure 6.13 Scheme of heme synthesis showing sites of lead effect. PBG, porphobilinogen; UROPOR III, uroporphyrinogen III; COPRO III, coproporphyrinogen III; PROTO, protoporphyrin; CoA, coenzyme A, ALA, aminolevulinic acid; CYTO C, cytochrome c. Source: Goyer and Ryne. Reprinted with permission from International Review Experimental Pathology. (c) Academic Press, Inc., 1973.

cadmium - only lead significantly influences the ALAD activity of red blood cells. Lauwerys, et al., (1973) suggest that further investigations of various parameters (e.g., age, pregnancy, drugs) which may influence ALAD are justified as well as those on any biological significance of the inhibition of this enzyme.

Lauwerys, et al., (1974) investigated the relationship between urinary delta-aminolevulinic acid excretion and the inhibition of red cell delta-aminolevulinate dehydratase by lead. They used venous blood collected in heparinized tubes from 83 male workers occupationally exposed to lead and from 84 control workers. ALAD activity decreased exponentially as a function of PbB concentration. The coefficient of correlation between log ALAD and PbB (in the range 0 to 75 micrograms per 100 milliliters PbB) was -0.76, confirming previous reports. The results indicate the threshold for ALA excretion is at a PbB Level of 45 micrograms per 100 milliliters. This confirms earlier studies in industrial populations (Selander and Cramer, 1970) and in children (National Academy of Sciences, 1972) indicating a PbB threshold for elevated ALAD of approximately 40 micrograms per 100 milliliters.

The average ALAD concentration at a PbB concentration of 45 micrograms per 100 milliliters was 37 percent higher than that found at a PbB concentration between 10 and 20 micrograms per 100 milliliters. When PbB exceeded 45 micrograms per 100 milliliters, ALAD increased rapidly. At a PbB of 55 micrograms per 100 milliliters, its concentration was already twice that found at a PbB level of 10 micrograms per 100 milliliters (Lauwerys, et al., 1974).

Different characteristics of erythrocyte ALAD between workers with a history of occupational lead exposure and normals were observed by Tomokuni (1975). In the blood of lead workers, when the hemolysates were heated at 60 C for 5 minutes, the activity of the erythrocyte ALAD increased up to about 3.6-fold times initial level and the optimum in pH-activity curve changed from pH 6.0 to 6.6. On the contrary, in normal blood, the optimum in the pH activity curve was but little changed by the same heating process, even though the erythrocyte ALAD activity was increased up to about 1.3-fold of the initial level.

Secchi and Alessio (1974) and Haeger-Aronsen, et al., (1971) showed that there is an inverse relation between blood-lead levels and erythrocyte ALAD in individuals with diverse occupational exposures to lead. Weissberg, et al., (1971) demonstrated that many children living in slum housing had elevated blood-lead levels and decreased red cell ALAD levels. Lead workers examined at different intervals following the cessation of lead exposure exhibited a rapid return to normal urinary ALA levels (within 4 months), but ALAD levels were only 25 percent normal at 4 months, and 80 percent at 16 months (Haeger-Aronsen, et al., 1974).

The effect of blood-lead concentration (PbB), age, sex and time of exposure upon erythrocyte aminolevulinic acid dehydratase (ALAD) activity was investigated by Tola (1973) in 1,370 workers (1,199 men, 171 women) under different conditions of exposure to lead. A close negative correlation was observed between blood lead (PbB) and ALAD in 1,147 workers. Furthermore, the ALAD activities in groups arranged according to PbB values (see Tables 6.9 and 6.10) show the close relationship between PbB and ALAD.

PbB had a statistically significant effect on the ALAD levels in workers. The exposure groups were significantly different from one another in ALAD activity (p less than 0.001) when PbB intervals of 10 micrograms per 100 milliliters were utilized. At PbB-intervals of 10 micrograms per 100 milliliters, the differences between the groups were statistically significant only up to the 60 to 69 micrograms per 100 milliliters PbB group, reaching a level of maximum depression from 70-100 micrograms per 100 milliliters. No difference was observed between the ALAD activities at the same blood-lead levels in men and women. Duration of exposure exerted an effect independent of PbB, such that the ALAD activity was lower after less than one year's exposure than in exposures of longer duration. ALAD activity was found to be higher in the age group of 24 years or less than at more advanced ages, controlling for blood-lead levels. Measurements were made of the blood hemoglobin in 1,269 workers, and of ALAD in 285 workers (see Tables 6.11 and 6.12). The hemoglobin level did not differentiate between PbB groups, and was not correlated with PbB and ALAD.

Blood-lead levels and erythrocyte ALAD activity in people living around a secondary lead smelter were investigated in 1970 by Nordman, et al., (1973). There was a statistically significant negative correlation between PbB and the distance of habitation from the emission source and a positive correlation between the PbB's and the monthly dustfall lead within the area. Higher levels of PbB closer to the emitting source were accompanied by a decrease in ALAD activity. ALAD proved to be a useful test in the demonstration of even a low-grade increase in lead absorption.

Secchi, et al., (1974) studied the delta-aminolevulinic acid dehydratase (ALAD) activity of erythrocytes and of liver tissue in subjects not occupationally exposed to lead. A considerable heterogeneity in the levels of ALAD activity of erythrocytes was confirmed in this group of subjects, an expression of the individual variability in lead absorption from lead in food and the atmosphere. In the group of 22 subjects studied (both sexes, between 24 and 69 years of age), there was a correlation between the values of erythrocyte ALAD activity and the values of ALAD activity of liver tissue. This correlation of erythrocyte and liver ALAD activity had been reported earlier for suckling rats by Millar, et al., (1970). The above research demonstrates again that ALAD inhibition is a useful index of lead exposure.

Baboon studies showed that while blood-lead concentrations increased very slowly during a chronic oral regimen of lead salts, ALAD decreased to a minimum value immediately (Goldstein, et al., 1975). The continued intake of lead had no further depressant effect on ALAD activity following the first day of treatment.

Table 6.9 ERYTHROCYTE δ-AMINOLEVULINIC ACID DEHYDRATASE (ALA-D) ACTIVITIES IN DIFFERENT BLOOD-LEAD (Pb-B) GROUPS[a]
(grouping at Pb-B intervals of 10 μg/100 ml)

Pb-B μg/100 ml	ALA-D μmol PBG/h/1 RBC														
	Men					Women					Total				
	n	$\bar{x}$	x—SD	x+SD	p[b]	n	$\bar{x}$	x—SD	x+SD	p[b]	n	$\bar{x}$	x—SD	x+SD	p[b]
≤ 9	5	721	370	1405	ns[b]	11	1033	818	1304	ns[b]	16	923	600	1419	ns ••
10—19	182	941	663	1325	< 0.001	71	952	697	1300	< 0.001	253	944	673	1324	< 0.001
20—29	327	716	490	1046	< 0.001	34	646	446	934	< 0.001	361	709	486	1034	< 0.001
30—39	161	507	332	775	< 0.001	8	260	161	421	ns[b]	169	491	314	770	< 0.001
40—49	108	353	210	595	< 0.001	9	258	206	324	ns[b]	117	345	207	575	< 0.001
50—59	67	226	139	366	< 0.001	4	263	194	363	< 0.05	71	228	142	366	< 0.001
60—69	43	146	73	295	ns[b]	6	146	95	227	ns[b]	49	146	75	286	ns[b]
70—79	45	121	67	216	< 0.001	8	91	48	173		53	116	64	209	< 0.001
80—89	32	77	38	154	ns[b]	1	125	..	..		33	78	39	155	ns[b]
90—99	15	58	30	110	ns[b]	1	25	..	..		16	55	28	105	ns[b]
100≤	9	49	25	94		..	..	..	..		9	49	25	94	

[a] Source: Tola (1973) Reprinted from Work, Environment, Health.
[b] p-value of difference between the mean ALA-D activities of the successive Pb-B groups.
[c] ns = not significant ($p > 0.05$).

Table 6.10 ERYTHROCYTE δ-AMINOLEVULINIC ACID DEHYDRATASE (ALA-D) ACTIVITIES IN DIFFERENT BLOOD-LEAD (Pb-B) GROUPS[a]
(grouping at Pb-B intervals of 20 μg/100 ml)

Pb-B μg/100 ml	ALA-D μmol PBG/h/l RBC														
	Men					Women					Total				
	n	x̄	x—SD	x+SD	p[b]	n	x̄	x—SD	x+SD	p[b]	n	x̄	x—SD	x+SD	p[b]
≤19	187	935	652	1341	< 0.001	82	962	721	1302	< 0.001	269	943	668	1330	< 0.001
20—39	488	639	417	979	< 0.001	42	543	320	922	< 0.001	530	631	407	977	< 0.001
40—59	175	298	173	516	< 0.001	13	260	204	332	< 0.001	188	295	173	504	< 0.001
60—79	88	133	70	253	< 0.001	14	112	61	203	< 0.001	102	130	68	245	< 0.001
80≤	56	66	33	132		2	56	..	..		58	66	33	131	

[a] Source: Tola (1973). Reprinted from Work, Environment Health.

[b] p-value of difference between the mean ALA-D activities of the successive Pb-B groups.

Table 6.11 HEMOGLOBIN VALUES IN DIFFERENT BLOOD-LEAD (Pb-B) GROUPS, SEPARATELY FOR MEN AND WOMEN[a]

Pb-B µg/100 ml	Hemoglobin g%					
	Men			Women		
	n	x	SD	n	x	SD
≤ 9	5	14.5	1.7	11	12.4	1.6
10—19	238	14.8	1.0	72	13.5	0.9
20—29	373	14.9	1.0	36	13.8	1.0
30—39	178	15.0	1.0	9	13.6	1.0
40—49	116	15.0	1.0	9	13.1	0.9
50—59	70	15.0	1.0	4	14.1	0.8
60—69	44	14.9	1.0	6	13.0	0.8
70—79	41	14.7	1.0	7	12.0	0.7
80—89	29	14.4	1.0	1	10.2	..
90≤	17	14.8	1.4	1	12.0	..

[a] Source: Tola (1973). Reprinted from Work, Environment, Health.

Table 6.12 CONCURRENT MEASUREMENTS OF ERYTHROCYTE δ-AMINOLEVULINIC ACID DEHYDRATASE (ALA-D) ACTIVITIES AND URINARY δ-AMINOLEVULINIC ACID (ALA-U) CONCENTRATIONS IN DIFFERENT BLOOD-LEAD GROUPS[a]

(285 workers)

Pb-B μg/100 ml	n	ALA-D μmol PBG/h/l RBC			ALA-U mg/l		
		x	x—SD	x+SD	x	x—SD	x−SD
≤ 9	..	..	..	..	..	..	..
10—19	12	978	645	1483	6	4	8
20—29	31	741	481	1143	7	6	10
30—39	20	479	332	690	6	4	9
40—49	43	315	179	551	6	3	13
50—59	51	204	128	324	10	6	18
60—69	38	158	82	305	11	5	23
70—79	47	109	62	191	18	8	38
80—89	27	83	44	155	28	13	58
90≤	16	46	24	89	32	11	95

[a] Source: Tola (1973). Reprinted from Work, Environment, Health.

Hammond (1973) investigated the effect of EDTA (ethylenediaminetetraacetate) on the activity of delta-aminolevulinic acid dehydratase (ALAD) and the excretion of lead in the urine of lead-intoxicated rats. Inhibition of ALAD was greater in blood than in liver, and EDTA treatment of rats given lead gave rapid reactivation of ALAD in the liver but had little effect on lead-induced ALAD inhibition in the blood. EDTA-induced lead excretion in the urine was inversely proportional to the liver ALAD activity.

Garber and Wei (1973) found that ALAD activities of three mice strains used in their investigation were significantly different, and suggested that this was due to genetic control of the rate of enzyme synthesis rather than different enzyme characteristics. The results indicate that inhibition of delta-aminolevulinic acid dehydratase activity is not related to acute or subacute lead toxicity as measured by lethality, body weight loss, liver and kidney weight changes or decrease in hematocrits.

The reversal of the ALAD deficit in lead-poisoned erythrocytes has been demonstrated *in vitro* with reduced glutathione (GSH). *In vivo* administration of GSH to workers with lead-intoxication improved the decreased erythrocyte ALAD activity to some extent, which would be expected since the endogenous GSH concentration in erythrocytes is known to decrease moderately in workers intoxicated with lead (Roels, et al., 1975). These investigators compared the *in vivo* effect of inorganic lead and cadmium on glutathione reductase system (GSH) and delta-aminolevulinate dehydratase (ALAD) in human erythrocytes in 84 men employed in a Belgian cadmium- and lead-producing plant. A control group of 26 persons was also examined.

The logarithm of the PbB was found to be significantly negatively correlated with log ALAD activity ($r = -0.760$) and with GSH ($r = -0.423$). Log CdB was associated with neither ALAD nor GSH activity. An *in vivo* investigation of the GSH regeneration rate of intact erythrocytes demonstrated that the overall activity of the glutathione oxidation-reduction pathway is not impaired in lead- and cadmium-exposed workers with significantly increased PbB and CdB. This suggests that the moderate decrease in endogenous erythrocyte GSH in lead-exposed workers might result from lead-induced impairment of the erythrocytic mechanism for glutathione synthesis (Roels, et al., 1975).

Persons with depressed levels of ALAD who exhibit no overt signs of lead toxicity may be developing subclinical symptoms of toxicity. Since ALAD in circulating erythrocytes has no known synthesizing or other functions, it is questionable if lead inhibition of this enzyme is toxicologically important. However, ALAD deficits which occur in brain and liver following lead exposure may be very important as the synthesis of heme-containing respiratory enzymes depend on ALAD (Millar, et al., 1970; Secchi, et al., 1974).

Chisolm, et al., (1975) studied a group of 18 children, 14 of whome had blood-levels above 50 micrograms per 100 milliliters but none of whom had symptoms of lead toxicity. Linear relationships were found among urinary lead and EDTA-chelatable lead (indicators of lead dose), and the indicators of heme synthesis depression (urinary delta-aminolevulinic acid and erythrocyte protoporphyrin). Blood-lead levels did not correlate well with either indicator of lead's effect on heme synthesis. The authors suggest that the use of the chelatable lead-test (urinary lead following calcium-EDTA treatment) is the best measure of soft tissue lead concentrations, superior to measures of PbB.

Many believe the determination of free erythrocyte porphyrin (FEP) or zinc protoporphyrin (ZPP) to function as screening tests for excessive lead exposure. The correlation between FEP or ZPP and PbB is moderately good. Correlation coefficients between FEP and PbB of 0.65, 0.9 and 0.77 have been obtained in children (Chisolm, et al., 1975; Piomelli, 1973; Lamola, et al., 1975) and a correlation coefficient of 0.87 was obtained by Lamola, et al., (1975) in adults. Correlation is improved when the lead exposure conditions are stable owing to the fact that the appearance of protoporphyrin in the blood reflects an event which occurred earlier in the bone marrow, before the erythroid cells reached the blood. (Sassa, et al., 1973).

In addition to serving as useful screening tests for lead exposure, elevation of protoporphyrin reflects an undesirable effect of lead on hematopoiesis. It is reasonable to consider the accumulation of an essential metabolite, e.g., protoporphyrin, as a critical effect. That is, accumulation of protoporphyrin is probably an indicator of disturbed funtion due to lead absorption.

Marginal elevation of FEP may represent a compensatory increase in heme synthesis. Blood hemoglobin decrements only occur at lead exposure levels somewhat greater than the threshold levels for a rise in FEP. Thus, the data of Pueschel, et al., (1972) and of Betts, et al., (1973) show that a lead-related fall in blood hemoglobin in children is seen only as PbB rises above 40. Tola, et al., (1973) noted a slight drop in blood hemoglobin related to lead exposure in industry with PbB's of approximately 50 micrograms per 100 millileters.

A threshold for increased erythrocytic protoporphyrin has not been adequately defined. Piomelli (1973) estimated a PbB threshold of 40 micrograms lead per 100 milliliters in children. On the other hand, Roels, et al., (1975) estimated a threshold of 20-30 in women and children and 25-35 micrograms per 100 milliliters in men. In the lead air quality criteria document (U.S. Environmental Protection Agency, 1977) average thresholds (lowest-observed effect levels) proposed on the basis of a number of studies were 15 to 20 micrograms per 100 milliliters in children and 20 to 25 for adult males.

Also in the EPA document it is argued that while certain of the initial hematological effects (such as ALAD inhibition) constitute relatively mild, non debilitating symptoms at low blood lead levels, they nevertheless signal the onset of steadily intensifying adverse effects as blood lead levels increase. Thus, elevation of free erthyrocyte protoporphyrin is suggested as a significant early measure of lead exposure.

If these estimates are correct and if elevation of erythrocytic protoporphyrin is to be viewed as a critical effect, the exposure level (PbB) at which it occurs would represent the lowest critical effect yet found.

6.3.2.3 Nervous System Toxicity--

6.3.2.3.1 Pathology--The pathological lesions noted in lead-induced CNS anomalies include cerebral edema, encephalopathy, increased cerebro-spinal fluid pressure, proliferation and swelling of endothelial cells, dilation of capillaries and arterioles, glial cell proliferation, focal necrosis, and neuronal degeneration (Goyer and Rhyne, 1973). These conditions, however, do not differentiate between symptomatology and/or pathology due to alkyl lead from that of inorganic lead. This section will focus primarily on inorganic lead neurotoxicity, leaving organic lead toxicity to be discussed separately in Section 6.6.

Lead encephalopathy is the most serious acute manifestation of lead intoxication. It rarely occurs in adults and only following the rapid absorption of large amounts of inorganic lead. Children are much more susceptible to lead-induced neuropathy than are adults (see Section 6.3.2.3.5). Acute lead encephalopathy usually has a sudden onset, typically with intractable seizures, followed by coma and cardiorespiratory arrest. In fatal cases, death usually occurs within 48 hours of the initial seizure unless life support is provided. The prodroma may include paralysis or weakness, sluggishness, poor memory, and hyperirritability. The onset and course of symptoms are unpredictable and may abate if the patient is removed from the source of lead (National Academy of Sciences, 1972). A source of lead which has been implicated in causing adult encephalopathy in the U.S. is "moonshine" whiskey. Whitfield, et al., (1972) studied such patients and found that many exhibited symptoms ranging from confusion to repeated seizures, coma and death. Most had anemia; lateralizing, neurologic signs were observed in 35 percent of the patients. Pentschew (1965) autopsied patients who had died from lead encephalopathy and found no cerebral edema in 3 out of 20 cases. This author points out that swelling of capillary endothelial cells and astrocytic proliferation are the most common features in lead encephalopahty. Cerebral edema may result from the convulsive episodes which accompany the intoxication.

Neuropathological changes were produced in suckling mice by adding 0.5 to 1.0 percent of lead carbonate to the diet of the maternal animals immediately after they had given birth (Rosenblum and Johnson, 1968). Intoxicated neonates displayed faulty growth and development, and revealed hematologic evidence of lead intoxication. Neuropathologic findings included abnormally large numbers of fibrous, intercapillary strands in several cerebral loci, and astrocytosis in the hippocampus. The latter was recognied most easily in sections stained with phosphotungstic acid hematoxylin. In addition, metallic impregnations for astrocytes and microglia revealed consistent differences between experimental and control material suggesting a general alteration in the properties of glia and/or cerebral tissue of intoxicated mice. In addition to the study by Rosenblum and Johnson (1968), important papers on experimentally induced, and histopathological evaluation of, lead encephalopathy in different species include: (1) Pentschew and Garro (1966); (2) Lampert (1966); (3) Thomas, et al., (1971); (4) Thomas and Thomas (1974); (5) Clasen, et al., (1974); (6) Krigman, et al., (1974); (7) Bouldin and Krigman (1975); (8) Thomas, et al., (1973); (9) Wells, et al., (1976); (10) Hopkins and Dayan (1974).

The histological findings in suckling mice differ from those of suckling rats (Pentschew and Garro, 1966). Studies using maternal transfer of lead to developing neonates to study the effect of lead on brain have been critically reviewed by Michaelson (1973).

Patel, et al., (1974) describe the effect of inorganic lead on metabolic compartmentation in the 19-day-old rat brain. Lead was ingested by suckling rats through the milk of mothers fed a diet containing 4.5 percent lead acetate. Assessment of metabolic compartmentation of brain amino acids was made by comparing the metabolism of [2-^{14}C]-glucose and [^{3}H]-acetate which were injected simultaneously into the suckling rats. Changes in the rate of conversion of both precursors into amino acids associated with the tricarboxylic acid cycle were observed.

In the brain of young rats ingesting lead, the specific radioactivity of glutamate, aspartate, gamma-aminobutyrate and glutamine were all significantly lowered relative to that of glucose. Glutamine labelling was the most affected. In comparison with controls, the total amount of ^{3}H in either water or acid-soluble constituents of the brain was the same, but the ^{3}H content of the amino acids was significantly reduced in the lead-treated rats. In both groups, glutamine had the highest specific radioactivity but the time courses of the labelling of glutamine were different. In spite of the differences in the metabolism of [^{3}H]-acetate, metabolic compartmentation of glutamate, assessed by a glutamine: glutamate-specific radioactivity ratio higher than 1, was evident even in the brain of the lead-treated animals, although the values of the ratio at 5 and 10 minutes were less than in controls. There was no evidence of a diminished supply of substrates to the brain in lead intoxication. The overall changes in this study were consistent with a retardation in the biochemical maturation of the brain in terms of development of glucose metabolism and metabolic compartmentation (Patel, et al., 1974). Michaelson (1973) indicates that the regimen employed leads to low body weights of animals suckling from mothers fed lead acetate. This depressed body weight has been cited by all investigators using the Pentschew and Garro (1966) model for getting lead into a suckling developing neonate. Few investigators have controlled for the contribution of undernutrition in these lead studies. A retardation in the age-dependent increase in the conversion of glucose carbon into amino acids was observed in studies in the brain of undernourished infant rats (Balazs and Patel, 1973).

In a study undertaken to determine the growth retardation in mouse pups exposed to lead and to determine the effects in brain development, Maker, et al., (1975) observed a dose-related retardation as high as 50 percent of controls in body growth, brain development, and sexual and behavioral maturation (see Figure 6.14). Although dams fed 0.4 percent or more of lead (as lead acetate or carbonate) ate less than control mice, this investigation concluded that undernutrition is apparently not the major cause of retardation since varying the litter size did not greatly modify the detrimental effect of the diet. However, it is known that varying litter size has little effect on growth rate of pups until you exceed 10 pups per dam so comparing 3 pups vs 6 pups as described by Maker, et al.,(1975) does not contribute to the resolution of the question. Small brain size and retardation of bone growth were characteristic in the lead-fed mice (see Figure 6.15).

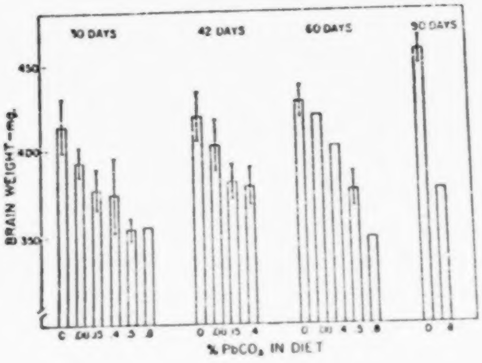

Figure 6.14 Brain weights of C57/BI/6J mice at 30, 40, 60, and 90 days of age raised on diets containing 0, 0.08, 0.15, 0.4, 0.5, or 0.8 percent lead (carbonate) for 60 days after birth. The standard deviation of mean brain weights are indicated.

[a]Source: Maker, et al. Reprinted with permission from Environmental Research. (c) Academic Press, Inc., 1975.

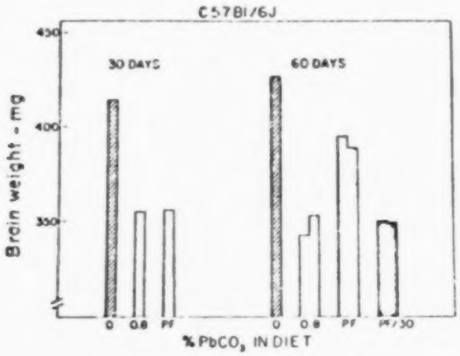

Figure 6.15 Brain weights of C57/BI/6J mice at 30 and 60 days of age raised on diets containing 0 or 0.08 percent lead as $PbCO_3$ for 60 days after birth are compared to those of a litter (PF) pair fed. At 30 days, 2 of the pair-fed pups were allowed an ad libitum diet containing 0.8 percent lead carbonate. The brain weights of these pups after 30 days on this diet (i.e., at age 60 days) are shown (PB/30).

[a]Source: Maker, et al. Reprinted with permission from Environmental Research. (c) Academic Press, Inc., 1975.

Golter and Michaelson (1975) found that the daily oral administration of lead acetate solution (1.09 milligrams of lead) to suckling rats does not influence growth relative to coetaneous controls and that lead-exposed animals show periods of increased motor activity. Endogenous levels of brain dopamine were unchanged whereas norepinephrine was increased, this suggests a possible relationship between lead exposure during earliest developmental periods, increased motor activity and brain norepinephrine, rather than brain dopamine.

Hopkins and Dayan (1974) investigated the pathology of experimental lead encephalopahty in two adult and one infant baboon. Lead carbonate was given by repeated intratracheal injections under light anesthesia. The main pathological findings were widespread edema and focal cortical necroses. The mechanisms by which lead produces these changes were not identified. Hopkins and Dayan (1974) unfortunately do not adequately describe experimental protocols, exposure levels, timing of exposure, blood lead levels, brain lead levels and how this relates to the 3 deaths out of the 15 animals who originally entered the study in 1970.

Clasen, et al., (1974a)administered lead subacetate (0.5 gram) and 1000 units of Vitamin D to 4 newly weaned rhesus monkeys three times a week. Between 6 and 18 weeks the animals suddenly developed ataxia, nystagmus, generalized weakness and convulsions. The authors claim that this experimental model resembled acute encephalopathy seen in humans more closely than encephalopahty experimentally produced in the rat; Clasen, et al., did not provide information as to the basis for the difference of opinion on this point between their work and that of Pentschew and Garro (1969), however.

Lead poisoning was diagnosed in four primates by finding toxic amounts of lead in tissues (Sauer, et al., 1970). Abnormalities in the brain and spinal cord were characterized by vascular lesions and demyelination. These finding suggest a new animal model for the study of demyelination and strengthen the supposition that lead may be a factor in some idiopathic demyelinating diseases. A preliminary report which suggests this possibility concerns the accidental poisoning of four primates who had suffered from accidental lead intoxication for various lengths of time before death in the Washington, D.C. Zoo. A detailed study of a larger number of similar cases is reportedly being prepared for publication. Dr. B. C. Zook of the Washington Zoo and George Washington Medical College has recently published a number of significant papers on experimental lead poisoning in primates.r an accidental poisoning of four primates in which accidental lead intoxication existed for various lengths of time before death occurred in the Washington, D.C. Zoo. The authors do state that "A detailed study of a larger number of similar cases is being prepared for publication." Between the time of this paper (1970) and the preparation of this document (1977) Dr. B. C. Zook of the Washington Zoo and George Washington Medical College has published a number of significant papers on experimental lead poisoning in primates.

6.3.2.3.2 *Neuromuscular and synaptic transmission effects*--Both organic and inorganic lead have been found to interfere with the transmission of nerve impulses and, therefore, neuromuscular function. Investigations dealing primarily with inorganic lead compounds will be discussed here; studies relating to alkyl lead compounds will be discussed separately in the organic lead section (6.6.4).

Silbergeld, et al., (1974a and 1974b) presented evidence for a junctional effect of lead on neuromuscular function. To separate the effects of lead on nerves from the effects on muscle, these investigators carried out *in vitro* studies of isolated phrenic-nerve diaphragm preparations from male Sprague-Dawley rats. The diaphragms with both phrenic nerves attached were removed from the rats and separated into two hemidiaphragms, each with a nerve trunk attached. The nerve-muscle preparation was modified so that preparations could be stimulated separately either through the nerve or muscle. One hemidiaphragm with its phrenic nerve was exposed to lead, as lead chloride, in a range of concentrations from 1 x 10^{-5} M to 1 x 10^{-4} M. Its pair was run simultaneously as a control. Krebs-Ringer-bicarbonate solution was used in all experiments. The most significant finding was that lead and calcium might interact at the presynaptic (junctional) level and thereby alter the metabolism of acetylcholine. Studies were also conducted on nerve-muscle preparations from mice chronically exposed to lead acetate added to their drinking water (Silbergeld, et al., 1974b). The studies from exposed animals are questionable since exposed animals were only 60 percent of their normal weight and similar studies using weight-matched mice were not conducted. The experiments demonstrated that lead, in concentrations greater than 1 x 10^{-5} M significantly decreased the force of contraction of the rat hemidiaphragm muscle on phrenic nerve stimulation (see Table 6.13). The latency between nerve stimulation and contraction was also increased. Over the same range of concentrations, the force of contraction was not affected when the muscle was stimulated directly (Silbergeld, et al., 1974a and 1974b).

Silbergeld, et al., (1974b) found that the effects of lead on force of contraction and latency were dose- and time-related. Responses to exogenous acetylcholine or acetyl-beta-methylcholine were not affected by lead. These results suggest that lead does not significantly interact with motor end-plate receptors to change the response to the neurotransmitter acetylcholine. Therefore, the *in vitro* effects of lead, at least, are confined to prejunctional sites of the peripheral motor nerves. The electrical properties of the nerve and/or transmitter function may be involved in the induction of these effects. Such effects may be responsible for the production of ataxia, muscle weakness and paraplegia in both animals and humans chronically exposed to lead.

The authors stated that phrenic nerve hemidiaphragm preparations taken from mice chronically exposed to lead were found to be functionally different from preparations taken from unexposed mice of the same age. Muscles from exposed animals generated a significantly smaller force of contraction on stimulation of either the nerve or the muscle. Since the experiment did not control for undernutrition, it is conceivable that this mode of response is characteristic of undernourished animals independent of lead exposure.

Table 6.13 EFFECT OF LEAD ON THE FORCE OF CONTRACTION ON NERVE AND MUSCLE STIMULATION AFTER TREATMENT FOR 2 HOURS[a]

Concentration of Lead (x 10^{-5} M)	n	Percentage of Initial Force of Contraction on Stimulation through: Nerve	Muscle
0	15	97.5 ± 2.5[b]	98.0 ± 2.0
1	4	97.5 ± 2.5	98.0 ± 2.0
5	3	77.8 ± 9.7	97.5 ± 2.5
8	6	60.8 ± 5.4	97.5 ± 2.5
10	1	47.7	96.5

[a] Source: Silbergeld, et al. Reprinted with permission from Nature. (c) Macmillan; Ltd. (1974).

[b] Mean ± s.e.m.

Whereas the Silbergeld studies used physiologic measures (i.e., force of contraction and latency), Manalis and Cooper (1973) employed electrophysiologic measures to monitor intracellular responses from individual end-plates such as frequency of miniature end-plate potentials. Manalis and Cooper (1973) demonstrated that lead influences both pre- and postsynatpic events in neuromuscular transmission with the presynaptic ones being most sensitive. Experiments were performed *in vitro* on isolated sciatic nerve satorius muscle preparations of the frog (*Rana pipiens*). Superficial neuromuscular junctions were located optically with a compound microscope (magnification x 400). Standard microelectrode and phtotgraphic techniques were used to monitor intracellular responses from individual end plates. Responses were recorded first while the preparation was bathed in a control Ringer's solution, then in the presence of lead, added as $PbCl_2$, and finally after the lead had been washed out. Acetylcholine was applied directly to the end-plate receptors by iontophoresis from a micropipette in order to test for post-synaptic effects of lead.

These investigators observed that lead increases the frequency of miniature end-plate potentials. As is the case with other ions which inhibit the phasic release of the neurotransmitter, it is not known with which ligands of the presynaptic membrane lead combines. If this were known some insight might be gained concerning the involvement of these ligands in excitation-secretion coupling. The salient features in this report were: (1) lead effects on evoked transmitter release were greater than on spontaneous release and (2) in agreement with other workers, the effect of lead is primarily presynaptic and not on the postsynaptic or neuromuscular function. Furthermore, the threshold end plate potential was reduced by 0.01 M lead within less than one minute whereas no significant increases in the frequency of the miniature end plate (mep) potentials were detected when this amount of lead was added to normal Ringer's Solution.

It is interesting to note that Manalis and Cooper (1973) reported that 0.01 M (2.1 ppb) produced measurable effects and this concentration is quite comparable to that of Silbergeld, et al., (1974a,b) who showed that lead concentration greater than 1×10^{-5} M (0.01 mM, 2.1 ppb) significantly decreased the force of contraction. Thus, there appears to be some agreement as to the moles concentration of lead needed to elicit this neuromuscular physiological effect.

Kostial and Vouk (1957) studied the perfused superior cervical ganglion of the cat to study the effect of lead (5-40 micromoles) on synaptic transmission and on the release of acetylcholine from preganglionic nerve endings. They found that lead in concentrations as low as 12.1 micromolar (1.21×10^{-5} M) blocked ganglionic transmission and reduced the output of acetylcholine. The release of acetylcholine or the uptake of choline and subsequent synthesis of choline is known to have a requirement for calcium ions (Katz and Miledi, 1967). Kostial and Vouk is one of the earliest papers in this line of research to show that calcium ions (10 mM) relieve the block produced by lead ions and restored acetylcholine output.

Relative to the introduction of Pb^{++} and Ca^{++} Kober and Cooper (1976) studied the interaction of lead and calcium and presented data which infers that lead competitively inhibits Ca^{++}-mediated transmitter release from presynaptic terminals. This was suggested by experiments in which the effects of lead on the uptake of ^{45}Ca by presynaptic terminals resulted in a three-fold increase in $^{45}Ca^{++}$ uptake. ^{45}Calcium uptake of stimulated lead-blocked ganglia was reduced by 91 percent (to 9 percent) of control, indicating that lead strongly blocks the uptake of calcium normally associated with the arrival of action potential at the presynaptic nerve terminals.

From this and the work of others a model for the mechanism by which lead interfers with normal neutronal activity is emerging. This is that lead blocks transmission by competitive antagonism of spike-evoked entry of Ca^{++} into presynaptic terminals and a subsequent reduction of transmitter release.

6.3.2.3.3 Peripheral neuropathy--Goyer and Rhyne (1973) and Haley (1971) have reviewed the literature and found peripheral neuropathy to be one of the more common manifestations of chronic lead toxicity in adults. Lead-induced peripheral neuropathy or "lead palsy" is manifested by motor weakness of the extensor muscles of the hands or feet, resulting in "hand drop" or foot drop. Lead neuropathy may be bilateral, although it is usually unilateral. Other muscles which are affected are the extraocular muscles of the eye. In an early clinical study of neuropathy in lead-poisoned adults, nearly two-thirds of 55 patients were found to have some degree of muscle weakness and almost one-half had wrist drop (Thomas, 1904).

Although peripheral neuropathy is considered to be one of the more common symptoms of chronic lead toxicity in adults (Goyer and Rhyne, 1973) children may also develop peripheral neuropathy with chronic lead poisoning. Whereas wrist drop is the most common manifestation of lead neuropathy in adults, foot drop and generalized weakness are more common in children (Seto and Freeman, 1964). Altered peripheral nerve conduction velocity has been reported in adults with 1 to 17 years of industrial exposure and whose Bl-Pb never exceeded 70 micrograms/100, as discussed in detail below by Seppalainen, et al., (1975). Similar altered peripheral nerve conduction velocity in chronic lead-intoxicated children has been reported by Feldman, et al., (1973). In this instance conduction velocity was measured in children known to have had one or more of the following: (1) Blood-Pb greater than 40 micrograms/100 ml, (2) U-Pb greater than 600 mg/24 hr following acetic acid provocation, (3) radiographic evidence of lead lines or radiopaque flecks in the gastrointestinal tract. It has been recently postulated that children with sickle cell disease have an increased risk of developing neuropathy with exposure to lead. Clinical documentation to support this belief has been provided by Erenburg, et al., (1974), Anku and Harris, (1974) and Athreya and Oski, (1975). Whether skeletal muscle is directly affected by lead remains unresolved. Early investigators suggested that lead produced a primary myopathy but lead content of skeletal muscle in lead intoxication is usually not very high. Also, electromyography of affected patients does not show a myopathic pattern (Preiskel, 1958). Experimentally it has been shown that lead ions reduce the output of acetylcholine and that calcium reverses this effect of lead. Whether lead affects ganglionic transmission in man is not known. Haley (1971) mentions reports which suggest that the neuromuscular lesions result from the degenerative, neural action of lead, or from the selective damage of blood vessels supplying the nerves. These suggestions stem from Russian, Indian, Italian, and German reports and deserve careful evaluation.

Knowledge of the lesions in lead-induced peripheral neuropathy has evolved from study of experimental models beginning in the 1880's with the observation that guinea pigs with chronic lead intoxication develop a peripheral neuropathy characterized by segmental degeneration of myelin sheaths. Recent extension of these experiments by Fullerton (1966) has confirmed the frequent occurrence of segmental demyelination and of axonal degeneration. Lampert and Schochet (1968) and Schlaepfer (1968, 1969) have shown that in rats segmental demyelination and remyelination are related to Schwann cell degeneration and proliferation. Schlaepfer (1969) has also demonstrated Wallerian degeneration of posterior nerve roots of sciatic and tibial nerves, which suggests a cellular basis for lead-induced parethesia and sensory nerve loss. Similar loss of nerve structural integrity has been reported in the 8th nerve of guinea pig (Gozdzik-Zolnieckiewicz, and Moszyriski, 1969) and the vestibular system of the adult squirrel monkey (Wilpizeski, 1974). Ganglion cells show no consistent pathological alterations, but surrounding capsular cells contain increased numbers of organelles and dense bodies (Schlaepfer, 1969). A detailed clinical description in adult lead industry worker has been provided by Seppalainen and Hernberg (1972) and Seppalainen, et al., (1975).

Subclinical neuropathy was studied in 39 male lead workers, of which 31 had a diagnosis of poisoning but all were without clinical signs of neurological impairment (Seppalainen and Hernberg, 1972). Standard electromyograms revealed abnormalities (fibrillations and/or diminished number of motor units) in 24 men. The mean maximum conduction velocities (MCV) of the ulnar and median nerve were significantly lower in the group of lead workers as compared with an age-matched control group. The conduction velocity of the slower fibers (CVS) of the ulnar nerve proved to be a very sensitive indicator of lead damage. A combination of this variable and the distal latency of the median nerve discriminated lead workers from controls better than any other combinations. The findings were consistent with slight neuropathy, and show that lead also affects certain portions of the fibers in the proximal part of the nerve.

The lack of correlation between the severity of subclinical nerve damage and the intensity of lead effects suggests that nerve damage is produced independently of other manifestations of poisoning. There is a dearth of information on the value of present acceptable limits of lead exposure from the point of view of the nervous system.

Catton, et al., (1970) obtained evidence in a group of lead battery workers of subclinical peripheral nerve fiber damage without clinical evidence of a neurological lesion. Of the 19 men examined, 13 had blood levels about 80 micrograms/100 milliliters and 7 had hemoglobin levels below 12 grams/100 milliliters, showing that considerable exposure to lead was occurring.

Some relationship was found between the peripheral nerve damage, length of exposure to lead, and the presence of anemia, but there was little relationship with blood-lead levels. In this respect, the neuropathy behaved like anemia of lead poisoning, which other workers have found to correlate poorly with the blood-lead level (Williams, 1966).

Several of the symptoms of amyotrophic lateral sclerosis (muscle fasciculations, proximal girdle atrophy) are seen in lead industry workers suspected of having motor neuron disease. In spite of suggestive clinical evidence (Campbell and Williams, 1969) a cause and effect relationship between lead and motor neuron disease has not been established (Currier and Haerer (1968).

Petkau, et al., (1974) found that lead levels in neural and muscular tissues were significantly elevated in patients with this disease, regardless of whether or not they had previous occupational exposure to lead.

The findings of normal lead concentrations in the lead-containing compartments of humans with multiple sclerosis would indicate no association between multiple sclerosis and lead poisoning (acute or chronic). The effects of lead might be induced by mobilization therapy (Westerman, et al., 1974). The complexities of this issue are discussed by Hammond in the National Academy of Sciences document (1972). Also, there has been another recent paper by Conradi, et al., (1976) on the topic of abnormal tissue distribution of lead in myotrophic lateral sclerosis. In this study, the lead content of cerebrospinal fluid was found to be significantly elevated 2.84 ± 1.19 (range 1.56 to 5.30) when compared to 28 control subjects having non-degenerative neurological disorders (1.41 ± 0.49 micrograms/100 grams (range 0.89 to 2.61).

6.3.2.3.4 Behavior effects--A recent NIOSH report (Repko, et al., 1975) examined 80 behavior parameters and five measures of body burden of lead in industrial workers (Table 6.14). The experimental group consisted of 316 individuals employed in lead storage battery companies, and the control group was derived from workers of similar age, sex, race, education, but with no occupational exposure to lead.

The following are the salient points in their findings:

(1) Blood ALAD activity was a better indicator of functional capacity than were blood lead levels, urinary Pb, ALA, or coproporphyrins. Decreasing levels of blood ALAD correlated with decreased auditory acuity and eye-hand coordination, increased muscular tremor, and decreased endurance/strength ratios in men with 70 micrograms Pb per 100 millimeters of blood or above.

(2) Of the intellectual functions tested, none indicated a decreased capacity in their experimental group. The authors, however, suggested in retrospect that

Table 6.14 SUMMARY OF FUNCTIONAL CHANGES IN WORKERS EXPOSED TO INORGANIC LEAD[a]

Test Area	Functional Category	Predictors of Criterion Performance		Significant Correlations	Change in Functional Capacity	
		Primary	Secondary		Direction of Change	Indicated PbB Level[b] Where Change Occurs
Signal Detection	Watchkeeping	Age	Education	-----	-----	-----
Pattern Discrimination	Sensory-Perceptual	Age	Education	-----	-----	-----
Mental Arithmetic	Intellectual	Education	Age	-----	Decrease	-----
Visual Acuity	Sensory	Age	-----	-----	-----	-----
Auditory Acuity	Sensory	Age	ALA	PbU, PbB, ALA-D	Decrease	80-89μg%
Tremor	Neuromuscular	ALA-D	-----	ALA-D	Decrease	70-79μg%
Muscular Strength, Endurance & Recovery	Neuromuscular	ALA-D	PbU	PbU[c], PbB, ALA-D	Increase	70-79μg%
Eye-Hand Coordination	Neuromuscular	Age	Employment	PbU, ALA-D	Decrease	70-79μg%
Immediate Recall	Intellectual	Education	-----	-----	-----	-----
Subjective Feelings	Psychological	Employment	-----	-----	Decrease	70-79μg%

[a] Adapted from Repko et al.,(1975).

[b] PbB--Blood lead.

[c] PbU--Urine lead.

these particular tests were not appropriate for industrial workers (one test being too easy, the other too difficult).

(3) In psychological tests, significant increases in hostility, depression, and general dysphoria were detected in lead workers as compared to controls. No biochemical parameter correlated with these particular observations.

Behavior dysfunction usually occurred in workers with blood-lead levels of 70 micrograms per 100 milliliters or above. Blood ALAD levels are inversely related to blood lead concentrations, and are more sensitive indicators of functionality. Therefore, it was recommended that a combination of blood ALAD activity below 21 units, and a blood level above 70 micrograms per 100 milliliters be used as an indicator for further evaluation of a worker's medical status. Another alternative is to remove the worker from the lead environment. Whether these criteria are appropriate for other individuals in high-lead environments deserves further consideration.

Several criticisms of Repko, et al., (1975) deserve mention. First is the possibility that biased responses on questionnaire items were evoked due to the prior information the subjects were given concerning the purpose of the study. For example, each volunteer was given complete and comprehensive explanation of the study including the expected results of the research. Information obtained from such preconditioned subjects is apt to be biased in the direction of these expected results.

Second, it should also be noted that audiometric tests were conducted without the use of a sound chamber and with ambient background sound levels of 65 - 80 dbA. Although audiologists would not consider this good practice for testing auditory acuity, neither lead-exposed nor non exposed workers should have been affected preferentially by a test administered to both groups under adverse conditions.

In addition, one could dispute some of Repko, et al's,, (1975) interpretation of the psychological tests. For example, the authors concluded that lead workers had significant increases in hostility, depression and general dysphoria over controls. Interestingly, however, individual subjective states for anxiety, depression and hostility indicate no significant relationship existed between Multiple Affect Adjective Check List (MAACL) and the clinical measures for either the experimental or control group. There was also a great deal of variability in the data of all MAACL measures. The relationship between blood lead and the psychological measures employed was by no means uniform. The dysphoria measure showed a saw tooth effect when plotted. Peak dysphoria effects occurred at 70 and 100 micrograms/100 milliliters while troughs were seen at 60 and 90 micrograms/100 milliliters lead in blood. Clearly, there is no apparent explanation for the phenomenon from a physiologic standpoint. Repko's findings are best regarded as speculative until further research under better methodological conditions is carried out.

McCallum (1972) discusses the possible health effects of lead in the environment on adults. He recommends the use of a battery of psychological tests in men exposed to a known lead hazard, but without clinical poisoning. These tests would be geared to detect early symptoms of lead poisoning and would be related to blood lead levels, urine coproporphyrin, and ALA excretion.

Bryce-Smith and Waldron (1974b) have presented a review on the neural and behavioral toxicity of lead in children and adults. The authors obtained information from: (1) prisoners who have elevated blood-lead and urinary-ALA values; (2) hyperkinetic children with abnormal lead metabolism and who often respond to EDTA therapy; (3) lead workers who underwent personality and behavioral changes; and (4) experimental animal models. They concluded that lead probably is a significant causative factor in the antisocial bahavior of children and adults. Unfortunately, the work of Bryce-Smith is not original research, but rather a highly selected collection of papers and personal communications. The document states that the authors obtained information from: (1) Prisoners who have elevated blood lead and urinary-ALA values - what is not brought out in this document is that Bl-Pb and U-ALA were determined in two different prison populations, the former in Switzerland (Lob and Desbaumes, 1971) and the latter in America, (Barnes, et al., 1972). Where Bl-Pb was done U-ALA was not; where U-ALA was done Bl-Pb was not. What the document also doesn't bring out is that Lob and Desbaumes subsequently (1976) retracted the 1971 report and concluded that the blood lead levels obtained in 1971 by polarography were too high. The mean actual value determined by AAS for prisoners does not differ significantly from the value for the non-occupationally exposed population. Lob and Desbaumes go on to state, "Unfortunately the blood lead concentrations published in our 1971 paper were taken by other authors (Bryce-Smith, 1972, Bryce-Smith and Waldron, 1974b as supporting the hypothesis relating lead and blood to anti-social and criminal behavior."

In connection with the second point, that hyperkinetic children with abnormal lead metabolism often respond to chelation therapy, Bryce-Smith and Waldron, 1974a) are referring to the work of David (1976) which in fact does not substantiate claims made by Bryce-Smith and Waldron (1974a) (based on earlier personal communication with David) that chelation therapy has been found to cure hyperactive behavior in children.

Conclusion: Within the past 5 years a considerable volume of literature has developed on neonatal lead exposure, brain development, neurochemistry, and behavior. Controversy exists as to the meaningfulness of this research. There are serious flaws in experimental design, and many secondary effects (i.e., nutritional status) confused the results and make objective evaluation of these data difficult. More recent preliminary studies (abstracts) report opposite findings or no change in catecholamines. Protocols for exposure are so varied that definite conclusions for lead effects on brain neurotransmitters must await more meaningful experimentation.

6.3.2.4 Immune System Toxicity--

There is little evidence on the impairment of immunologic mechanisms from lead, as reviewed by de Bruin (1971). Lead-treated animals, subsequently subjected to active immunization, develop lesser quantities of gamma-globulin than normal (control) animals. The activity of lysozyme seems to be reduced progressively in the spleen and blood serum of dogs poisoned by the prolonged administration of inorganic lead salts. In a group of employees in a lead-processing plant, the mean activity of lysozyme was found to be subnormal, and the lowest values were found in the most severely affected persons. The immunologic impairment of lead is reflected by a decreased Vitamin C content in the adrenal gland.

Studies by Drs. Rafael Trejo and Nicholas Di Luzio suggest that the accumulation of lead in the lysosome appears to be sufficient to disrupt its activity, to the point at which it can no longer detoxify endotoxin (Anon., 1971). Later work by these same investigators demonstrated that enhancement by lead of endotoxin lethality is not due to impaired phagocytosis but rather to some effect on endotoxin detoxification. (Trejo, et al., 1972).

Koller and Kovacic (1974) found that chronic exposure of mice to lead (as lead acetate) in drinking water (1375, 137.5, or 13.75 ppm) produced a significant decrease in antibody synthesis, particularly IgG, indicating that the memory cell is involved. There was a reduction in the number of spleen cells producing 19S or IgM antibody at each dose of lead. The largest dose resulted in a fivefold decrease in antibody-forming cells as compared to the controls, but even those mice receiving the lowest dose had a significant decrease in the number of 7S or IgG plaque-forming cells. Rabbits given 2,500 ppm lead as lead acetate in drinking water for 70 days and then inoculated with pseudorabies virus as the antigen had significantly lower neutralizing antibody titers (marked immuno-suppression) than did the controls (Koller, 1973). These results indicate that reduced antibody synthesis may be responsible for the increased mortality from bacterial and viral diseases in animals that are chronically exposed to lead.

Lead decreases normal responsiveness to bacterial endotoxins in rats as evidenced by increased mortality rates following *Salmonella enteritidis* endotoxin administration (Cook, et al., 1974). When lead and *E. coli* endotoxin were administered to baboons in doses which were individually subtoxic, morphologic changes appeared in their livers suggesting a synergistic, toxic action of the two agents (Hoffman, et al., 1973). Cook, et al., (1975) reviewed the effects of lead on endotoxin-induced pathology. When rats are dosed with 5 milligrams of lead acetate per rat (a dose which equals one-tenth the LD_{50} for 300-gram rats), the dose of bacterial endotoxin that would kill 100 percent of the population is 2,000 to 10,000 times less than for rats receiving no lead. Young rats are more sensitive to such interactions than are adult animals. Schroeder (1973) also noticed that male rats and mice fed 25 micrograms of lead (as lead acetate) per liter in drinking water had a higher susceptibility to bacterial infections.

Mice exposed to daily doses of 100 and 250 micrograms of lead nitrate in 0.5 milliliter of saline for 30 days showed greater susceptibility to challenge with *Salmonella typhimurium* than controls which had received no lead (Hemphill, et al., 1971). There was a tenfold difference in the LD_{50} of the S. typhimurium organisms between the control and the lead-treated mice. The susceptibility of the lead-treated mice to a strain of S. typhimurium with limited pathogenicity was markedly increased.

A single, normally well-tolerated, intravenous injection of lead acetate (5 milligrams) increased the sensitivity of rats to the endotoxins of various gram-negative bacteria about 100,000 times above normal (Selye, et al., 1966). Under the conditions of the experiments used, the mortality and organ changes normally produced by the intravenous injection of 100 micrograms of E. coli endotoxin were essentially the same as those obtained by use of one nanogram in lead-sensitized rats. The sensitizing effect of lead acetate for E. coli endotoxin was greatest when the two agents were given simultaneously.

Viral-induced diseases in mice were aggravated by administering lead acetate in the drinking water (Gainer, 1974). Mortality from viral inoculations was higher in lead-treated mice than in controls. In addition, lead-pretreated mice exhibited splenomegaly following viral inoculations (Rauscher virus) and higher mortalities. Large titers of virus were recovered from the spleens of the lead-treated animals. The suggested mechanism for this action is that lead antagonizes interferon synthesis, thus lowering natural defenses to viral infections. Goyer and Rhyne (1973) point out that proof of such a relationship may be difficult to establish in affected humans.

Many people die per year in the U.S. from Gram-negative bacteremia and endotoxemia, but no epidemiological studies have been reported on the relative risks of such infections to people with increased lead exposure.

6.3.2.5 Cardiovascular System Toxicity--

Concern in the past that lead contributed to hypertension and other cardiovascular diseases in humans was most prevalent when industrial hygienic measures surrounding lead workers were unregulated. The review by Goyer and Rhyne (1973) mentions reports of myocardial abnormalities in acutely intoxicated children. In a followup study (based on regular control over 20 years) of 364 lead workers in a battery factory, Cramer and Dahlberg, (1966) found that regular health examinations and good working conditions resulted in an incidence of hypertension not greater than that found in the general population.

There is epidemiological evidence that heavy industrial lead exposure at one time caused increased incidence of death from cerebrovascular disease (cerebral hemorrhage, thrombosis and arteriosclerosis) (Dingwall-Fordyce and Lane, 1963). The increased incidence of death from this class of diseases was associated with a degree of lead exposure which probably no longer exists. A more recent epidemiological study of causes of death among lead workers does not indicate any excess deaths due to cerebrovascular diseases (Cooper and Gaffey, 1975). The workers studied were not as heavily exposed as earlier workers, but the vast majority had PbB's greater than 40 micrograms per 100 milliliters. Thus, it seems highly unlikely that lead is responsible for deaths at the exposure levels which are experienced by the general population.

An association between the accumulation of lead in aortas and severe atheromatous lesions has been observed in humans (see Section 6.2.2), but no causal relationship has been established. Studies of lead-induced atherosclerosis in experimental animals have also been inconclusive. Increased serum lipoprotein and cholesterol, and cholesterol deposits in the aorta have been reported with heavy lead exposure in rats and rabbits (Sroczynski, et al., 1967). Others, however, have failed to produce athersclerotic lesions using similar doses of lead in rabbits (Prerovska, 1973).

6.3.2.6 Endocrine system Toxicity--

The clinical effects of lead on the hematopoietic, neuromuscular, and renal systems coupled with the adverse biochemical phenomena which have been observed suggested to Sanstead (1973) that lead may also impair the function of the endocrine system. Standard tests of endocrine function on the thyroid, pituitary, adrenal cortex, and juxtaglomerular apparatus of patients who had acquired their lead by drinking moonshine indicated impairment of function in many cases. Six of eighteen patients demonstrated a decreased excretion of pituitary gonadotrophic hormones. Nine of sixteen had low (less than 10 percent) 24-hour thyroid uptakes of iodine. Three of them were hyporesponsive to thyroid-stimulating hormone. The adrenal response to exogenous ACTH was decreased in five of ten while eight of twenty excreted low amounts of 17 OHCS following oral metapyrone. Plasma cortisol levels were low in seven of eight given metapyrone. Two of four metapyrone nonresponders were also poorly responsive to insulin hypoglycemia. In contrast, growth hormone responses to hypoglycemia were normal in eight. The renin-aldosterone response (see Section 6.3.2.1) to acute sodium deprivation was impaired in nine of eleven patients. Sodium deprivation for 10 to 28 days did not result in an appropriate increase in renin or aldosterone in four subjects.

The effect of lead ingestion (1 percent lead acetate) on *in vitro* steroid synthesis of the rat adrenal gland was investigated by Wright, et al., (1975). Blood-lead concentrations rose to 85 micrograms per 100 milliliters of whole blood in 1 week and stayed at or above this level for the 8-week experimental period.

Lead ingestion resulted in an increase in adrenal weight during the first 4 weeks of lead exposure, followed by a return to near control values. The net-percent conversion of ^{14}C-progesterone by adrenal tissue to 11-deoxycorticosterone, aldosterone, and deoxycortisol first rose, then returned to near or below control values, in a variable pattern, by the 8th week. The data suggest an initial stimulation of the adrenal gland function during the early stages of lead intoxication followed by either an adaptation by or an exhaustion of the adrenal. In contrast, de Bruin (1971) reports on research in which steroids were found to decrease during the initial period of the lead poisoning of animals, but increased considerably during advanced stages of intoxication.

Absorption of lead appears to exert a depressing effect upon the thyroid gland (de Bruin, 1971). Sheep poisoned by prolonged lead absorption in increased quantities have been found to have an abnormally low level of protein-bound iodine, an indication of reduced thyroid activity. According to de Bruin no protein-bound iodine observations have been made in connection with the occupational exposure of humans to lead.

6.3.3 Factors Influencing or Modifying Toxicity

Goyer and Mahaffey (1972) and Mahaffey (1974) listed age, season of the year (body temperature, dehydration, ultraviolet light), dietary calcium and phosphorus, iron deficiency, dietary protein, dietary Vitamin D, ascorbic acid, alcohol, other metals, coexistent diseases, and the intracellular complexing of lead (see Section 6.3.1) as factors that influence the susceptibility of humans and other animals to the toxic effects of lead. Some of these parameters are outlined in Table 6.15. Some factors cannot be controlled (age, season, some diseases), while others such as diet and living in high-risk lead environments can be.

Six and Goyer (1970) investigated the influence of lowered dietary calcium on a variety of biological parameters in rats fed a dose of lead (200 ppm lead acetate) which does not produce subclinical lead toxicity when accompanied by a lab chow diet. Lowering dietary calcium at the above lead dosage greatly increased the body burden of lead as was shown by increased absorption and urinary excretion of lead and increased lead levels in blood, soft tissue, and bone. Pathologic changes reflecting overt lead toxicity were greater in rats fed the low-calcium diet, including increased excretion of delta-ALA, increased frequency and size of intranuclear inclusion bodies and renal tubular cells, increased kidney size, and aminoaciduria.

Quarterman, et al., (1972) found that the susceptibility of rats to lead was increased severalfold by lowered calcium intake. A lowered phosphorus intake had a similar effect on lead retention in rats and the effects of calcium and phosphorus deficiency were additive. Transfer of lead from the mother to the newborn and to weanling pups was greater in the calcium-deficient rats. Although it has been reported that lead retention in rats cannot be decreased by increasing dietary calcium intake above normal requirements, addition of calcium and phosphorus to the milk ration of newborn rats has decreased their lead absorption (Quarterman, et al., 1972). On the other hand, milk itself enhances lead absorption in rats. (Kello and Kostial, 1973). The mechanisms underlying these interactions are presently unclear. There are, however, some similarities in calcium and lead metabolism. For example: Vitamin D also affects lead metabolism by increasing its blood and bone concentrations (Sobel, et al., 1940); lead and calcium distribution in the body are influenced in a similar manner by phosphorus (Potter, et al., 1971); and calcium and phosphorus occur with lead in intranuclear inclusion bodies (Carroll, et al., 1970). Furthermore, there is some similarity between the energy-dependent lead uptake by heart mitochondria and energy-dependent calcium accumulation (Scott, et al., 1971).

Although toxic manifestations of a certain lead dosage may be observed only with a calcium- or phosphorus-deficient diet, there is no evidence that the lead actually induces a deficiency state with regard to these elements. However, lead does cause some disturbance in the metabolism of these elements, with reductions in serum calcium (Six and Goyer, 1970).

TABLE 6.15. FACTORS INFLUENCING LEAD TOXICITY[a]

Factor	Correlation with Lead Toxicity	Species
Age	Negative	Human, rats
Season	Increased toxicity in summer vs. winter	Humans; increased temperature increased toxicity in rabbits and mice.
Dietary copper deficiency	Positive	Rats
Dietary calcium and phosphorus deficiency	Positive	Rats, humans?
Protein deficiency	Positive	Rats
Vitamin D excess	Positive	Rats
Vitamin C excess	Negative	Guinea pigs
Vitamin E deficiency	Positive	Rats
Nicotinic acid treatment	Negative	Rabbit, rats?, humans?
Drinking of alcohol	Positive	Humans
Iron deficiency	Positive	Humans, rats
Cadmium exposure	Positive	Rats
Diseases	All positive	Humans
Hemoglobin S or C		
Thalassemia		
Glucose-6-phosphate dehydrogenase deficiency		
Chronic renal disease		Humans, rats

[a] Compiled from Goyer and Mahaffey (1972); Goyer and Rhyne (1973); Klauder et al.,(1973); Levander et al.,(1975); McIntire and Angle (1972); and Quarterman et al., (1973).

Low-calcium and low-phosphorus diets greatly increased skeletal uptake of lead by adult female rats given 200 ppm lead acetate in the drinking water (Quarterman, et al., 1973). The subsequent release of this incorporated lead was strongly inhibited by low calcium diets. However, the uptake and release of lead was not related to the calcium:phosphorus ratio of the diet or to the degree of skeletal resorption or to the plasma calcium concentrations. The calcium and phosphorus content of the weanling carcasses was unaffected by the maternal diet.

Experimental studies suggest that absorption of lead varies as a function of age. Forbes and Reina, (1972) and Kostial, et al., (1971a,b) observed that nursing rats have a much higher absorption of lead when compared to adult rats. This may be related to the higher absorption of calcium in young rats.

Six and Goyer (1972) studied the synergistic toxic effect of low dietary iron and lead ingestion in rats which had been fed a subtoxic dose of lead (200 ppm lead acetate) in drinking water along with a purified diet containing adequate iron (25 ppm), calcium, and phosphorus, or a diet deficient only in iron (5 ppm). During the 10-week study period, there was a marked exacerbation of lead toxicity symptoms in the iron-deficient rats. The effects were similar to those reported for calcium-deficient rats except that, in this case, lead distribution between bone and soft tissues was not affected. Iron deficiency did result in an increased retention of lead in liver, kidney, and bone, and an increased urinary excretion of lead. Biochemical parameters of lead toxicity including urinary excretion of delta-ALA were greater in iron-deficient rats fed lead than in rats receiving adequate diets and lead.

There is no obvious explanation for the strong effect of iron deficiency on lead absorption and retention (Six and Goyer, 1972). There seems to be a common absorption pathway for iron, zinc, cobalt, and manganese (Forth and Rummel, 1971). In iron-deficient rats, absorption of these other elements is generally increased by two to three times, while the absorption of lead is much greater.

Calcium and iron intakes are most likely to be inadequate in children and pregnant women who are also found to be most susceptible to hematopoietic effects of lead and possibly to other effects as well. There is a need for further research to establish to what degree lead absorption and the manifestation of lead toxicity are affected in children consuming diets which are only marginally adequate in calcium, phosphorus, and iron.

One preliminary indication is that of Angle and Stelmak, (1975). They found that iron supplementation in children increases blood lead and that such supplementation does not alleviate the anemia differentially for high vs low blood lead children.

Mooty, et al., (1975) investigated the relationship of diet to lead poisoning in 46 children, aged 24 to 47 months (25 controls and 21 subjects) chosen according to low and high blood lead levels. The major finding in this study is that there was no significant difference in their protein, caloric or iron intake, leaving unanswered what factor(s) must account for the occurrence of lead poisoning in the subjects (see Section 8.3.1.6). On the other hand, lead absorption has been shown to be increased by high fat, low protein, and high protein diets, and decreased by high mineral diets (Barltrop and Khoo, 1975).

Thawley (1975) investigated the toxic interactions among lead, zinc, and cadmium with varying levels of dietary calcium and Vitamin D in rats. Male Sprague-Dawley rats (95 to 100 grams live weight) received dietary lead (0.5 percent), zinc (0.63 percent) and cadmium (90 ppm) individually and in combination with each other (the inorganic compounds supplying these metals were not given). These diets were eaten for 42 days with two levels of calcium (0.1 and 0.9 percent) and three levels of Vitamin D (0, 2,000, and 50,000 international units per kilogram of feed).

The most significant findings of this study were:

(1) A marked increase in the toxic effects, as well as blood, liver and kidney concentrations of lead, zinc, and cadmium in animals fed a calcium-deficient ration;

(2) A general increased toxicity of lead, zinc and cadmium as dietary Vitamin D levels increased from deficient to excess;

(3) An alleviation of the toxic symptoms (viz., increased ALA excretion and reticulocytosis) and a reduction of lead in blood liver, kidney, and bone by the concurrent administration of lead with zinc or lead with cadmium.

Reports that the incidence of swayback, a copper-deficiency syndrome in sheep, may be associated in some areas with elevated lead contents in pastures led to a study of the effects of lead on copper metabolism in rats. Klauder, et al., (1973) found that lead toxicity in rats was increased by a dietary deficiency of copper. They also had evidence for a protective role of copper in reducing lead toxicity, and conversely for a depressive effect which lead had on copper metabolism (see Figure 6.16 and Table 6.16). Ingestion of lead caused anemia in the low-copper rats (which was not evident in the rats receiving a normal amount of copper), reduced serum ceruloplasmin and copper in rats receiving the normal copper (with no depression of hemoglobin), and depressed zinc in rats getting low copper. Retention of lead in kidney and liver was inversely proportional to dietary copper levels. The very pronounced inverse relationship which was evident in all parameters (see Table 6.16) indicated a protective effect of copper at the higher levels. As shown in Figure 6.18, the amount of lead present in the erythrocytes of the rats, each of which was exposed to the 0.5 percent dietary lead, was inversely related to the amount of copper and ceruloplasm in the serum. This implies a mutual antagonism between these elements.

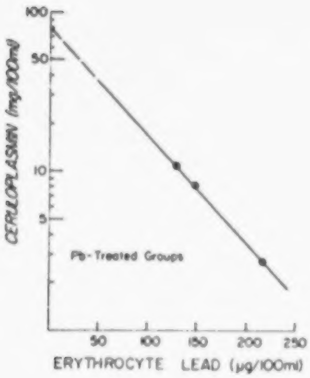

Figure 6.16 The effect of increasing ceruloplasmin levels on erythrocyte lead in male Sprague-Dawley rats fed a semipurified diet and 0.5% Pb for 56 days. The groups received 0.5, 1.5, and 2.5 μg Cu/g diet. Source: Klauder. Reprinted with permission from Proceedings 6th Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1973.

Table 6.16 EFFECT OF LEAD ON COPPER METABOLISM IN MALE RATS[a,b]

	Low Cu[c]	Normal Cu[d]	Low Cu +Pb[e]	Normal Cu + Pb[e]
Hematocrit (%)	48.5	51.4	36.2	51.2
Hemoglobin (g %)	12.2	13.2	8.1	12.3
Serum Cu (μg %)	6.0	57.2	7.5	12.4
Serum Zn (μg %)	138	124	98	121
Ceruloplasmin (mg %)	6.7	29.1	2.8	10.7

[a] Source: Klauder, et al. Reprinted with permission from Proceedings 6th Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1973.

[b] Parameters affected by lead acetate given in the copper-deficient semi-purified diet to male Sprague-Dawley (SD) rats for 56 days.

[c] Low copper diet contained 0.5 ppm Cu.

[d] Normal copper diet contained 2.5 ppm Cu.

[e] +Pb diet contained 0.5% Pb.

In contrast, Rubino, et al., (1958) showed that lead-exposed workers have increased erythrocyte-copper concentrations which is contradictory to what would be expected from the above results. He, therefore, believes that it is far from certain that a biologically significant copper-lead interaction exists, especially since the lead dosage used by Klauder, et al., (1973) was excessively high. Other reports of possible effects of lead on copper metabolism imply that some other copper-antagonist is responsible for the results obtained (Bremner, 1974).

Another possible interaction of copper and lead is a reduction in transplacental movement of lead when maternal copper levels are high (Baumslag, 1975). Willoughby, et al., (1972) found that young horses who were fed diets containing toxic amounts of lead and/or zinc had marked differences in clinical symptoms with the combined metals producing symptoms of zinc (but not of lead) toxicity. Tissue distribution of lead was altered by zinc intake; there was a large decrease in bone lead and increase in hepatic and renal lead concentrations. The finding of increased tissue lead content and decreased susceptibility to lead toxicity is as yet unexplained. The increased zinc intake almost certainly would have increased both renal and hepatic metallothionein content and may possibly have increased lead binding in this form with consequent detoxication, although Webb's (1972) data does not support this. Alternatively, the effect on lead metabolism may arise from effects of zinc on bone mineralization. It would be of interest to establish whether more physiological and nontoxic amounts of zinc can also offer protection against lead toxicity.

Alcohol ingestion has been implicated clinically as exacerbating lead toxicity. This apparent synergism might result from lowered nutrient intake by the alcoholic consumer, a metabolic interrelationship, or the presence of both lead and ethanol in illicitly distilled beverages (Anon, 1974). Mahaffey, et al., (1974) found that chronic consumption of ethanol by rats with controlled nutrient and energy intake during a 10-week study did not markedly affect the toxicity of orally ingested lead acetate (200 ppm). However, lead ingestion increased renal lead concentration from 0.7 ppm wet tissue to 6.4 ppm in the absence of ethanol and 16.6 ppm in the presence of ethanol. Ethanol increased the number of renal inclusion bodies in the kidneys of lead-eating rats. Bone and liver lead were not influenced by ethanol, and liver morphology was influenced by ethanol, but not by lead. It thus appears that any clinical synergism between lead toxicity and alcohol ingestion results from a lower nutrient intake or increased exposure to lead. Both lead and ethanol inhibit the enzyme aminolevulinic acid dehydrase, indicating some common biochemical effects. This has been reported in man and in rats (Moore, et al., 1971). Negative aeroionization reduces the toxic effects of lead (Straus, et al., 1973). Ninety rabbits were used to study the effect of lead (as lead acetate) administered intravenously, subcutaneously, or orally over 10 to 20 days, while simultaneously submitting the animals to moderate negative aeroionization. The experimental animals had lower mortality rate and a lower concentration of lead, and less alteration of the enzymes glutamino-pyuvic-transaminase in the serum, and cholinesterase in the blood.

Ghelberg, et al., (1973) investigated the effect of an anabolic therapy using methandrostenolone on white rats which had been given 950 milligrams of lead acetate per kilogram body weight in aqueous solution administered intraperitoneally over 7 months. A reduction of the concentration of lead was observed in the kidney, brain and femur, and improvements were noted in the serum fraction, and in the enzyme activity of the liver and the small intestine.

McIntire and Angle (1972) observed that black children who are deficient in the enzyme glucose-6-phosphate dehydrogenase have a higher lead concentration than those in whom the enzyme is normal. Since the serum lead concentration is actually lower than in normal children, this can be attributed to an increased binding of lead to the red cell.

6.3.4 Reproductive Effects: Fertility Reduction, Mutagenicity, Teratogenicity

The effects of lead on human reproductive functions per se have received little study in recent years. Consequently, much of what appears in the literature concerning human reproductive effects comes from very old studies of workers exposed to levels of lead orders of magnitude higher than today's lead workers, or alternatively from rather unscientific foreign reports of similar age. Lancranjam's (1975) study is the only recent investigation focusing exclusively on human fertility effects (specifically spermatogenic abnormalities) under reasonably well defined levels of lead exposure. Some cell culture studies of mutational activity of lead are also available.

Many laboratory animal studies are included in this section, therefore, because they serve as indicators of potential human effects and because the requisite human experimentation needed to clarify these effects is either unethical or absent. Nuclear polyploidy and abnormalities in mitosis have been noted in bone marrow cells by a number of investigators. Chromosomes from leukocyte cultures from mice fed a diet containing 1 percent lead acetate showed an increased number of gap-break type aberrations (Muro and Goyer, 1969). The observed chromosomal abnormalities largely involved only single chromatids. Failure to have a paired defect (break or gap) in both chromatids of a chromosome suggested that damage occurred after the deoxyribonucleic acid (DNA) synthetic phase of the cell cycle. There is a possible relationship between increased deoxyribonuclease activity and chromosome damage as a marked increase in DNA has been demonstrated in urine from lead-poisoned rats (Muro and Goyer, 1969). These findings are of interest with respect to the known effect of lead on reduction of fertility and possible oncogenesis and teratogenesis. Gap-break type aberrations of chromatids have been reported among lead workers having blood lead levels ranging from 62 - 88 micrograms/100 milliliters (Goyer and Rhyne, 1973). A variety of nonspecific changes in chromosome morphology (adhesions and spiralizing defects), and increases in tetraploid mitoses and the mitotic index were also noted.

The mutational activity of inorganic lead in lead workers was further examined by studying the chromosomes of cultured blood lymphocytes (Forni and Secchi, 1973). Significant increased rates of chromatid aberrations, and unstable chromosomal changes were seen in current workers as compared to controls or workers who had been removed from lead exposure for 18 or more months. None of the groups exhibited changes in stable chromosomes.

O'Riordan and Evans (1974) studied the extent of chromosomal damage, and correlation between the level of damage and the lead levels in blood and urine within a population of men occupationally exposed to oxides of lead. The population consisted of seventy male workers employed by a ship-breaking yard. Thirty-five men, aged 21 to 63 years (Group 1), were engaged as burners to cut the hulls and all metal structures of ships, and their lengths of exposure ranged from 3 months to 43 years with an average weekly exposure time of 50 hours. The remaining thirty-five men (controls) were of comparable age. Their findings (see Table 6.17) did not reveal any consistent and significant differences in the incidence of chromosome-type and chromatid-type aberrations between Groups 1 and 2 or among classes A, B, C, and D. Moreover, the results within any class were similar to those obtained from previous surveys of adult males from a variety of groups that were not considered to be unduly exposed to known or suspected mutagens.

Chromosomes from the peripheral blood lymphocytes of 14 workers from a zinc industry who showed signs of differing degrees of lead poisoning were studied by Deknudt, et al., (1973). According to the type and duration of exposure, the workers examined were classified into three groups: Group I: People exposed to a high level of zinc and low levels of lead and cadmium; Group II: People exposed to high levels of the three minerals; and Group III: People exposed to high levels of lead and cadmium in the absence of zinc. The aberrations observed were dicentrics, rings, chromatid exchanges as well as gaps and fragments. Exposure to zinc and cadmium did not seem to increase the number of cells with severe chromosomal anomalies. thus lead intoxication was considered to be responsible for these chromosomal aberrations.

Excess chromosomal breaks have been found in children suffering from lead poisoning, both acute and chronic (Shaw, 1970).

The older literature concerning industrial lead poisoning makes frequent reference to stillbirths, miscarriages and sterility among women working in the lead trades as well as among the wives of workers (Cantarow and Trumper, 1974; Oliver, 1914).

Lancranjan, et al., (1975) investigated the reproductive ability of men occupationally exposed to lead. They found that workmen having lead absorption ranging from slight to high (as judged by blood and urine analyses for lead, ALA and coproporhyrins) exhibited a substantial increase in spermatogenic abnormalities (asthenospermia, hypospermia and teratospermia). Although Leydig androgen function was not affected, germinal insufficiency appeared to result from a direct, toxic effect of lead on the gonads and did not occur through the hypothalamopituitary system. Studies with laboratory animals indicate that the ingestion of lead by either parent results in the reduction of both size and number of offspring.

Table 6.17 CYTOGENETIC FINDINGS IN CULTURED LYMPHOCYTES FROM SHIPYARD WORKERS WITH AN OCCUPATIONAL HISTORY OF LEAD EXPOSURE (GROUP 1), AND FROM SHIPYARD CONTROLS (GROUP 2) AND OTHER ADULT MALES[a]

					Cells with Chromatid Aberrations					Cells with Chromosome Aberrations				
Category	Blood Lead Level (ug per 100 ml	No. of Men Studied	Total Cells Scored	Percent Normal Cells	Total No.	Percent	Chromatid and Isochromatid Gaps	Chromatid Breaks	Chromatid Interchanges	Total No.	Percent	Dicentrics	Acentric Fragments	No. Structurally Abnormal Chromosomes[b]
A. Normal	<40	12 (Group 2)	1,200	91.5	51	4.25	53	0	0	5	0.42	2	5	0
B. Acceptable	40-80	16 (Group 1)	1,600	93.33	71	4.43	68	7	2	7	0.44	1	6	5
		17 (Group 2)	1,700	94.50	70	4.12	73	1	2	6	0.35	0	5	2
		33 (total)	3,300	94.47	141	4.27	141	8	4	13	0.39	1	11	7
C. Excessive	80-120	15 (Group 1)	1,500	93.87	72	4.80	68	5	0	13	0.87	0	7	3
		2 (Group 2)	200	94.29	10	5.00	10	1	0	1	0.50	0	1	0
		17 (total)	1,700	94.09	82	4.90	78	6	0	14	0.82	0	8	3
D. Dangerous	>120	4 (Group 1)	400	94.50	25	6.25	25	0	0	3	0.75	0	3	0
Total Group 1 (Exposed)	--	35	3,500	93.90	168	5.16	161	12	2	23	0.69	1	16	8
Total Group 2 (Control)	--	31	3,100	93.43	131	4.46	136	2	2	12	0.42	2	11	2
Other males[c]	--	285	3,107	96.66[d]	68	2.18	65	4	0	36	1.16	2	9	16

[a] Source: O'Riordan and Evans. Reprinted with permission from Nature. (c) Macmillan, Ltd. (1974).

[b] Number of structurally abnormal monocentric chromosomes observed which were not associated with an acentric fragment.

[c] Data obtained from previous MRC surveys of othe adult male groups with no history of undue exposure to known or suspected mutagens (lymphocyte culture time <

[d] Includes nonmodal cells.

Goyer and Rhyne (1973) cited a study in which the paternal ingestion of lead in rats resulted in the retardation of embryonic growth of offspring and reduced numbers of weaned pups per litter. While this may have been indicative of defective spermatozoa, no morphological or functional differences were noted between sperm from control and lead-fed parents. Maternal effects of lead were exhibited by reduced litter size, retardation of fetal development, and impaired postnatal survival. The ovaries of lead-burdened females (rats and rhesus monkeys) showed a reduced number of developing follicles.

When both male and female rats and mice were exposed to 25 ppm of lead (as lead acetate) in drinking water, the offspring had increased numbers of breeding failures, runts, young deaths and dead litters (Schroeder, 1973). Unspecified inorganic lead salts administered to pregnant mice and rats in low doses (25 ppm) in drinking water produced runting, reproductive failure and shortened life spans (Schroeder and Mitchener, 1971).

Hilderbrand, et al., (1973) investigated the effect of lead acetate on reproduction and metabolism in rats. Eighty sexually mature males and eighty sexually mature females were maintained in a controlled environment with a constant temperature of 25.5 C. The males and females were divided into three groups with each group containing 20 rats. Group 1 served as controls; Group 2 was treated orally with 5 micrograms of lead acetate for 30 days; and Group 3 was treated with 100 micrograms of lead acetate for 30 days. These dosages were presumably administered daily although the authors do not specifically say so. Results of this investigation revealed the following:

(1) In males, when the lead concentration in the blood increased from 14 to 26 micrograms per 100 milliliters, impotence and prostatic hyperplasia resulted.

(2) When the lead level increased to 50 micrograms per 100 milliliters, testicular damage occurred and spermatogenesis was inhibited.

(3) In the female, when lead concentration in blood increased from 14 to 30 micrograms per 100 milliliters, irregularity of estrus occurred.

(4) When lead levels reached 30 micrograms per 100 milliliters, persistent vaginal estrus occurred after normal estrus, and the development of ovarian follicular cysts with a reduction in the number of corpora lutea was noted.

(5) No toxicity or mortality occurred in the treated animals. Stowe and Goyer (1974) also observed that the reproductive performance of male rats is reduced as a result of lead exposure. The parentally transmitted effect includes reduction of litter size, weights of offsprings and reduced survival rates of the offsprings.

Teratogenic effects of lead have been demonstrated in experimental animals. Specific congenital-skeletal malformations were induced in golden hamster embryos by treating pregnant hamsters with lead acetate, lead chloride, and lead nitrate (Ferm and Carpenter, 1967). The malformations were primarily localized within the developing sacral and tail vertebrae and were characterized by varying degrees of tail malformations ranging from stunting to complete absence of the tail. Minor degrees of this malformation were compatible with life, and the fertility of several affected newborns which had been reared to adulthood did not appear to be affected.

Ferm (1969) injected female hamsters intravenously with cadmium sulfate (2 milligrams per kilogram) and lead acetate (25 and 50 milligrams per kilogram) on the 8th day of gestation. The combination of the metals revealed that the frequency and severity of clefts in the lip and palate usually caused by cadmium were reduced in the presence of lead, while the posterior tail malformations caused by lead appeared to be potentiated in the presence of cadmium. Ferm supports the possibility of cadmium and lead interacting additively on certain enzyme systems in the case of tail bud malformation and of lead blocking the effect of cadmium on the differentiating visceral arch system preventing the facial abnormalities. Ferm and Ferm (1971) showed that when female golden hamsters are given lead nitrate intravenously at a dose level of 25 or 50 milligrams per kilogram on the 8th and 9th days of gestation, the embryonic resorption and malformation rates rose with increasing doses of lead. Likewise, rats exhibited similar effects following the intravenous administration of lead nitrate to the dams (McClain and Siekierka, 1975). Interestingly, no such effects could be produced by oral feeding of lead. Fournier and Rosenberg (1973) found no significant teratogenicity in lead acetate-treated rats and rabbits over the controls.

McClain and Becker (1972) found tetraethyllead, tetramethyllead, and tetramethyllead chloride to be essentially nonteratogenic in Sprague-Dawley rats. Embryo or fetal toxicity was observed to accompany the administration of the organolead compounds and was characterized by growth retardation and delayed ossification of bone. Marked fetal effects were observed only in maternal animals that exhibited severe organolead toxicity and were, therefore, severely debilitated.

6.3.5 Carcinogenicity and Miscellaneous Biochemical Effects

Grandjean (1973) reviewed studies which suggest that lead and cancer are related. Some cancers were related geographically to elevated lead levels in soil and drinking water. Others showed that cancer patients had elevated levels of lead in the lungs and liver regardless of the site of cancer.

A followup of 425 workers exposed to lead in a storage battery factory was conducted by Dingwall-Fordyce and Lane (1963). They reported "no evidence to suggest that malignant disease was associated with lead absorption".

Similarly, a recent epidemiological study of causes of death among U.S. lead workers indicated that although deaths from neoplasms were higher than would be expected (based on the mortality rates among males in the general population of the U.S.), the incidence was not elevated to the point of statistical significance (Cooper and Gaffey, 1975).

In contrast to man, rodents are susceptible to lead-induced cancers. Sunderman (1971) reviewed reports of renal, adrenal, thyroid, prostate, and pulmonary adenomas, renal adenocarcinomas, and testicular carcinomas in rats and mice which had received lead phosphate, lead acetate, and basic lead acetate via dietary and/or parenteral routes. Lymphomas resulting from the subcutaneous injection of tetraethyllead were also reported.

Cerebral gliomas (usually poorly differentiated, malignant tumors) were induced in rats with dietary lead subacetate and 2-acetylaminofluorene (AAF) (Oyasu, et al., 1970). Twenty-five gliomas and 3 extracerebral intracranial tumors were found in 988 Wistar and caesarean-delivered (Sprague-Dawley) rats of which 663 were in experimental, and 325 in control groups. The tumors usually developed after 52 weeks of age. The highest incidence (8.6 percent) of gliomas was in animals ingesting lead subacetate and the difference compared with the incidence among controls, (0.3 percent) was statistically significant (P less than 0.05). In animals given 2-AAF (with or without olive oil, carbon tetrachloride, or ethionine) the incidence (2.5 percent) of gliomas was lower and their development was usually delayed until after 60 weeks of age but the incidence (5.5 percent) among rats that survived 60 weeks or more was statistically significant (P less than 0.05) when compared with that of 325 control rats in which only one glioma was found.

A similar interaction of lead and benzo-[a]-pyrene *vis-a-vis* tumorigenesis has been reported in hamsters (Kobayashi and Okamoto, 1974).

An increased incidence of lung cancer has been reported in lead, copper, and zinc smelter workers and in the residents of communities surrounding smelters (Anon, 1975a). However, the report adds that the arsenic emitted from these plants may be the actual cause of the cancer. Lead chromate has been linked to cancer in Europe (Anon, 1975b). The chromate ion has long been suspected as being carcinogenic (Furst and Haro, 1969), and is probably the active moiety in lead chromate. NIOSH is currently working on new criteria documents for lead and zinc chromates. Some paint manufacturers have also issued alerts concerning these pigments.

Martell (1975) postulates that tiny amounts of radioactive lead are absorbed by tobacco plants as they grow. The lead, he believes, is inhaled in the lungs with cigarette smoke, where it lodges and gives off alpha rays that destroy lung cells, or the radioactive lead particles spread throughout the body and cause some bone, stomach, and liver cancers.

Summarily, the entire issue of the carcinogenic potential of lead in humans must be considered unresolved.

Urbanska-Bonenberg and Smigla (1973) carried out clinical investigations and several routine biochemical examinations on 230 persons professionally exposed to inorganic lead and on several control groups. They concluded that the liver is somewhat resistant to lead and that under conditions of occupational exposure to lead, abnormalities of liver function may be due to other potentially pathogenic factors, for example, viral hepatitis and alcohol abuse. Abnormalities of liver function were also confirmed in rats subjected to subacute poisoning with lead acetate.

Numerous miscellaneous effects have been reported in the literature (e.g., elevated cholesterol levels in heavily lead-exposed humans and animals, modifications of proteins in blood serum albumin fraction, alpha, beta and gamma globulins in lead-poisoned humans and animals, shifts in metallic components of tissues and body fluids associated with changes in lead intake, etc.) These effects are reviewed by de Bruin (1971). The physiological significance of many of these effects, however, are totally obscure at the present time.

The affinity of lead sulfhydryl (-SH) groups (see Section 6.3.1) allows for reaction involving free thiol groups (e.g., glutathione) in the body. Such reactions spare certain enzymes to a greater or lesser extent. A reduction of the glutathione content of the erythrocytes in the presence of sufficient concentrations of lead has been observed both _in vitro_ and _in vivo_ (Bonsignore, 1967; Vergnano, 1967).

Related to the reaction of lead with thiol groups is the appearance of Heinz bodies which are formed by the oxidation of thiol groups bound to globin in hemoglobin. It is quite likely that there is a link between reduction in erythrocyte glutathione in lead exposure and the appearance of Heinz bodies since these result from the oxidative degradation of hemoglobin (Beutler, 1969).

It has been suggested that lead interferes with enzymatic degradation of tryptophan, of which 5-hydroxyindoleacetic acid (HIAA) is a final metabolite in a minor pathway. This metabolite was found in increased quantities in the urine of 227 children who lived in the vicinity of lead-processing industries. A well-defined relationship has been observed between the proportion of cases with increased urinary concentrations of HIAA and the concentration of lead in the air of the area (Ghelberg, 1966)The HIAA determinations were not quantitative and were not correlated with other indices of lead exposure. Others have noted a rise in urinary excretion of HIAA in moderate lead exposure (Urbanowicz, et al., 1969; Dugandzec, et al., 1973). Schicle, et al., (1974) on the other hand, were unable to find any significant elevation of HIAA excretion in a group of lead workers with levels of exposure greater than in the earlier studies.

6.4 LEAD TOXICITY IN CHILDREN

6.4.1 Unique Features of Lead Poisoning in Children

Considerable research effort has gone into the study of the features of lead poisoning unique to children. Although there are many such special features, they can be broken down into three categories: (1) Children have different modes of exposure than adults (e.g., eating non-nutritive lead-containing substances such as paint, dust, and soil). (2) The lead which is ingested seems to be absorbed at a higher rate than in adults. Also, children's developing nervous systems make them especially vulnerable to lead toxicity. (3) Manifestations of lead overexposure in childhood may include disorders of higher mental functioning (e.g., learning disabilities and hyperkinesis) which are effects unique to this group.

The exposure of children to lead has very unique characteristics. The vast majority of lead poisoning cases in children are due to eating leaded house paint (National Academy of Sciences, 1972). An important feature of this problem in preschool children is "pica" which is the repetitive ingestion of non-food materials. It has been suggested that the sweet taste of leaded chips reinforces this action. An essential element in lead poisoning risk for children is the age of the home. Older housing (30 years old or more) which is in disrepair gives easy access to paint peelings which may contain up to 40 percent lead by weight. Many articles have been written describing the problems associated with the childhood ingestion of leaded-paints (Hartman, et al., 1960; Griggs, et al., 1964; de la Burde and Shapiro, 1975; Jacobziner, 1966).

There are other sources of lead with a special relevance to children. These include street dust, surface or garden soil in areas of high traffic density, household dust, pencil, toy and furniture paint, improperly glazed earthenware, ashes from burning lead-battery casings, newsprint with leaded inks, toothpaste, and toothpaste tubes (Lin-Fu, 1973a,b; Eaton, et al., 1975; National Academy of Sciences, 1972). It should be noted, however, that the most significant source is still leaded paints (World Health Organization, 1977).

6.4.1.1 Sources--

To determine the relative contribution of different sources of lead, Lockeretz (1975) measured the lead content of teeth of children in five different environments in metropolitan areas. In each case, the mother lived in the area during pregnancy, and the child lived continuously in the same area until the tooth that was used in this study was shed. The five parameters studied were--lead paint, no lead paint, suburb, industrial, and public housing. Comparisons of populations based on lead levels in individual teeth showed the difference between areas with and without a lead paint problem, respectively, but showed no effects attributable to traffic density or industrial sources. Tooth-lead content was examined in children whose exposure to environmental lead differed with respect to four sources: lead paint; automobile exhausts; atmospheric industrial lead emissions; and mills. The only clear difference was that, in the area with a lead paint problem, children in both regular housing and in the projects had an average level almost twice as high as the other areas. In areas that have no lead paint problem no difference was observed between those that had high and low traffic densities.

Ter Haar and Aronow (1974) investigated the childhood lead problem in terms of (1) the major sources of lead in dirt around houses where children play, and (2) the extent to which children take in dust and air-suspended particles. Dirt was sampled at nine sites around each of 18 frame houses in widely scattered urban areas of Detroit. Dirt was also sampled around 7 farm houses in an area remote from traffic, located about 30 miles north of the nearest city, and about 50 miles north of Detroit. The data from the survey of the urban areas (see Tables 6.18 and 6.19) showed that the principal cause of elevated lead in the dirt in the yards is leaded paint on these houses. For the second part of the study, these investigators determined the amount of air-suspended particulate or dustfall a child might eat. They used a naturally occurring tracer, lead-210, which is present in dust but nearly absent from paint. The results (see Tables 6.20 and 6.21) showed that children with pica (and other evidence of high lead intake) and normal children excreted identical amounts of lead-210. Consequently, dust and air-suspended particulate were not the sources of lead in these urban children.

In an *in vitro* laboratory study of the lead in printed matter, Bogden, et al., (1975) found that dangerous quantities of lead, up to 200 micrograms, could be extracted from small pieces of printed paper at pH values in the range of human gastric fluid, i.e., 1 to 2. Lead was not extracted at pH values in the range of human saliva. Children who merely chew printed matter are not in danger of absorbing lead, but pica-prone children who swallow printed material may absorb toxic amounts of lead.

6.4.1.2 Absorption Patterns--

The absorption of ingested lead in children is believed to be more extensive than in adults (Section 6.2.1). Absorption coefficients for adults are in the range of 8 to 10 percent, while some children absorb up to 53 percent of ingested lead (Alexander, et al., 1973). It is clear that the relationship between environmental lead sources and blood lead will be different for adults and children.

The maximum daily permissible intake (DPI) of lead from all sources without excessive body-lead burden in children was at one time considered to be 300 micrograms (King, 1971). Barltrop suggested more recently that this figure should be 133 micrograms per day (Golz, 1973). King defines intake as the amount of lead ingested in the diet and nonfood substances, and the amount retained in respiratory exchange. Sources of data on which the DPI was based were:

(1) Levels of lead in the blood of exposed and nonexposed children and of those with frank lead poisoning;
(2) The results of experimental lead ingestion by adults;
(3) Measurements of fecal output of lead in exposed and nonexposed children;

Table 6.18 LEAD IN DIRT IN DETROIT[a]

House Type	House	Lead in Dirt, µg/g dry dirt								
		Within 2 Ft of House[b]				10 Ft from House		Near Sidewalk	Curb	Gutter
		Front	Back	Sides		Front	Back			
Painted frame	1	1919	3001	1170	748	985	351	449	660	596
	2	4121	674	7284	6003	536	289	1301	432	1079
	3	439	2193	1116	2548	278	608	326	610	508
	4	297	2539	1117	925	216	131	1482	680	n.d.
	5	920	2184	1211	1447	191	223	309	320	738
	6	126	233	186	916	58	157	343	321	1270
	7	n.d.	n.d.	1457	n.d.	n.d.	n.d.	627	404	645
	8	3420	n.d.	1380	5120	621	831	355	1957	1827
	9	179	372	611	1060	139	122	820	555	1047
	10	17590	4951	5552	7000	305	207	422	918	1387
	11	262	1585	5694	3402	197	219	506	338	1168
	12	295	292	140	104	170	149	152	220	n.d.
	13	556	246	446	254	229	285	266	328	1046
	14	1256	655	1206	4243	208	149	1958	331	550
	15	n.d.	162	1083	373	280	252	299	701	n.d.
	16	1077	1660	1894	1460	708	1220	425	419	935
	17	768	1094	220	1483	952	614	227	708	1277
	18	4068	3535	1452	1278	1530	1410	1017	400	415
	Average	2349	1586	2257	1846	447	425	627	572	966

Table 6.18 LEAD IN DIRT IN DETROIT[a]
(Continued)

		Lead in Dirt, µg/g dry dirt								
		Within 2 Ft of House[b]				10 Ft from House				
House Type	House	Front	Back	Sides		Front	Back	Near Sidewalk	Curb	Gutter
Brick	19	380	222	106	146	77	72	246	301	564
	20	606	168	217	128	125	94	438	711	1670
	21	78	169	96	1540	103	48	1130	431	2085
	22	1030	701	838	725	148	188	485	881	1360
	23	352	344	883	486	203	480	416	966	3170
	24	687	197	91	222	219	97	263	303	656
	25	104	107	194	95	88	75	87	147	1070
	26	183	1915	474	1210	312	329	248	324	578
	27	382	835	597	4610[c]	168	816	249	148	487
	28	377	283	1160	1500	228	163	403	2420	1410
	29	146	463	173	231	103	80	154	469	765
	30	146	203	102	269	108	84	169	330	600
	31	491	172	187	113	39	50	86	403	423
	32	140	72	1090	40	201	119	117	408	3140
	33	480	2350	800	632	316	417	301	395	867
	34	150	131	173	251	153	77	261	428	304
	35	366	442	218	281	111	244	317	750	2380
	36	227	243	276	2290	111	175	465	1210	298
	Average	351	501	426	595	156	200	324	612	1213

[a] Adapted from Ter Haar and Aronow (1974).

[b] Many of samples for painted frame house contained readily visible paint chips, especially house 10; n.d. denotes not determined.

[c] House next door was a painted frame house. This value not included in average.

Table 6.19 LEAD IN DIRT IN RURAL AREA: PAINTED FRAME FARMHOUSES[a]

House	Lead in Dirt, μg/g dry dirt 2 Ft From House[b]	10 Ft From House[b]	20 Ft From House[b]	Background
1	2162	417	67	9
2	450	429	144	27
3	6338	2093	166	26
4	1896	199	74	74
5	5184	556	640	12
6	840	428	107	63
7	831	141	268	94
Average	2529	609	209	44

[a] Source: Ter Haar and Aronow (1974). Reprinted from Environmental Health Perspectives.

[b] Each value is the average for four samples, one collected on each side of the house.

Table 6.20 LEAD AND LEAD-210 IN URINE[a]

Collection	Stable Pb, μg/l	^{210}Pb, pCi/l
1	147	0.23
2	153	0.28
3	121	0.74
	Treatment with D-Penicillamine (oral) began	
4	3820	0.27
5	1960	0.18
6	2030	0.42
7	6140	b
8	1400	0.27
9	2880	0.51
10	1170	0.48
11	3210	b
12	2530	b
13	1125	b
14	1780	0.40
	Treatment began with calcium disodium ethylenediaminetetra-acetic acid and 2,3-dimercapto-1-propanol (muscularly)	
15	4180	0.55

[a] Source: Ter Haar and Aronow (1974) Reprinted from Environmental Health Perspectives

[b] Sample was partly used in the hospital, leaving too small an amount for ^{210}Pb determination.

Table 6.21 LEAD AND LEAD-210 IN EXCRETA[a]

Normal Children		Hospitalized Children	
Stable Pb, μg/g dry	^{210}Pb, pCi/g dry	Stable Pb, μg/g dry	^{210}Pb, pCi/g dry
3	0.019	19	0.046
2	0.021	20	0.018
3	0.027	18	0.024
7	0.120	49	0.047
7	0.087	4	0.050
3	0.041	7	0.039
3	0.026	40	0.063
5	0.028	1640	0.037
4	0.044		
4	0.024		
Average	0.044	Average	0.040

[a] Source: Ter Haar and Aronow (1974). Reprinted from Environmental Health Perspectives.

(4) The initial effects of lead intake;
(5) Rates of increase in levels of lead in the blood of exposed children; and
(6) Sequelae of lead poisoning.

This daily permissible intake was developed at a time when it was not known that the absorption of lead from the gastrointestinal tract of children is considerably greater than that of adults. The rationale for it is therefore outdated. Various authors have more recently published data on fecal lead excretion of normal children and of children with abnormal lead exposure. On the basis of these data and assuming 40 to 50 percent absorption, it can now be specified that "normal" oral lead intake for children 1-5 years of age is approximately 10 micrograms/kg/day. An excellent review of these data is provided by Mahaffey, (1977).

Though definitive data are lacking, some estimate can be derived of the relative contributions of ambient air lead and dietary lead to total absorption. Table 6.22 presents estimates based on the studies of Alexander (1974) in children and of Rabinowitz (1974) in adults. The most notable aspect of Table 6.22 is that for normal, non-pica children, exposures to lead in ambient air accounts for a much smaller proportion of their total lead uptake than it does for adults (U.S. Environmental Protection Agency, 1976). For example, EPA calculated that an increment of 3 microgram/m^3 in ambient air lead concentration would result in an increase of 11 percent in average daily lead absorption in children. The same increment would result in an increase of 46 percent in average daily absorption in adults. For controlling body lead in an adult, diet and ambient air are approximately equal in importance; while for a child, diet is by far the more significant factor.

6.4.1.3 Manifestations: Learning Disabilities and Hyperkinesis--

Some manifestations of lead poisoning in children are quite similar to those in adults, and can be found in Section 6.3.2. Certain behavioral outcomes such as mental retardation and hyperkinesis are of particular interest in children.

The relation of blood-lead levels to cognitive and perceptual performance function was determined for 80 black preschool children (Perino and Ernhart, 1974). Their lead levels were below the criteria set for lead poisoning (not greater than 60 micrograms per 100 milliliters of blood), but regression analysis revealed that the effect of blood lead on performance was statistically significant. As the lead level increased, general cognitive, verbal and perceptual abilities decreased. Lead levels were not related significantly to parental intelligence, birth order, birth weight, and number of siblings.

This study provided a clear separation of the "study group" with elevated blood leads from low exposure "controls". Most previous studies of this type suffer from considerable overlap in the blood lead levels of the two groups. There was also a significant correlation between lead level and the amount of parental education. While results of this study are

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Table 6.22 RELATIVE CONTRIBUTIONS OF DIETARY AND AMBIENT AIR LEAD TO TOTAL LEAD ABSORPTION[a]

μg/Day-Person

Physiological Parameter	Airborne Lead, μg/m^3 2		Airborne Lead, μg/m^3 5		Δ Absorption With Δ + 3 μg Pb/m^3	
	Child[b]	Adult[c]	Child	Adult	Child	Adult
Intake						
Diet	159	360	159	360	--	--
Air	16	40	40	100	+24	+60
Total	175	400	199	460	+24	+60
Absorption						
Diet	82	33	82	33	--	--
Air	7	17	17	40	+10	+23
Total	89	50	99	73	+10	+23
Excretion						
Urine	51	38				
Hair, sweat	?	12				
Total	(63)	50				
Retention	(26)	0				

[a] Source: U. S. Environmental Protection Agency (1976).

[b] Alexander (1974).

[c] Rabinowitz (1974).

suggestive of a role of lead in intelligence performance, it may very well be that more highly educated parents are the underlying "cause" of both low blood lead (through regulating their children's behavior) and of superior mental functioning (through tutoring and more effective parenting).

Beattie, et al., (1975) conducted studies of the relationship between mental retardation and blood lead in Glasgow, Scotland, an area where extremely high levels of lead have been recorded in drinking water. One hundred fifty four children were examined, half of whom were classified as mentally retarded, and half were normal. The mean blood-lead level in the children tested was 25.4 micrograms per 100 milliters of whole blood compared with 17.8 for the controls and this correlated with the higher water-lead levels measured in the children's homes. None of the children from the control group came from homes with lead levels greater than 800 micrograms per liter, whereas eleven from the mentally retarded groups were exposed to as much as 2,000 micrograms per liter.

Another portion of the study looked at the effects of high lead concentrations (800 micrograms per liter or above) in Glasgow drinking water during pregnancy and in the first year following birth. They found that a strong correlation exists between high lead content and the development of mental retardation in the children from the age of 2 to 5. The combination of soft water and lead in plumbing contributed to the elevated levels in drinking water, both of which are preventable sources of lead (see Section 7.3.2).

There are a number of methodological issues which Beattie, et al., (1975) neglected, including matching of controls, confounding effects of social class, and comparison of biological parameters in the two groups. Until methodologically adequate studies are conducted, there appears insufficient justification for a claim that lead in drinking water causes mental retardation.

Landrigan, et al., (1975c) compared children between the ages of 3 and 15 years with blood lead levels of 40-60 micrograms per 100 milliliters to children with blood lead levels below 40 micrograms per 100 milliliters. Higher blood lead was weakly associated with lower I.Q. and slower motor skills, but was not associated at all with hyperactivity. Ethnicity and socioeconomic status were controlled in this study, but unfortunately age and sex were not. This tends to weaken the conclusions.

Another study found no relationship between blood lead and intelligence, reading ability, or hyperactivity (Landsdown, et al., 1974). Methodological weaknesses make both of the above studies somewhat suspect (World Health Organization, 1977).

Pueschel (1974) examined the neurological and psychomotor functions in 58 children with an increased lead burden 1-1/2 to 3 years after an in-depth study of various neurological and psychomotor functions was made. Of these children 23 to 27 percent had minor neurological dysfunction and various forms of motor impairment during each evaluation. While the initial psychological assessment showed low average mental abilities in the majority of children, a significant increase in certain areas of intellectual functioning was observed during a follow-up examination. Unfortunately, the control group was not administered any of the psychological tests, consequently no data is offered with which to compare the results of the 58 subjects. Although an improvement in certain areas of intellectual function is reported, there was no change with respect to neurologic evaluation of fine motor function or on the visual motor integration test.

de la Burde and Choate (1972) studied children exposed to a high-risk lead environment with a positive coproporphyrin test but no diagnostic signs of toxicity. They were found to have low IQ's, disturbed fine and gross motor performance, and suspect behavioral profiles. Unfortunately blood-lead levels or radiographic studies were not done on the children who served as controls.

Human studies relating lead to hyperactivity are linked to animal studies such as those of Silbergeld and Goldberg (1973, 1974) discussed in Section 6.3.2.4.

Lead ingestion in children has been linked to minimal brain dysfunction or "hyperkinesis" (David, et al., 1972; David, 1974b). Hyperactive children were compared with nonhyperactive controls on two measures reflecting the presence of body lead (blood lead levels and urinary-lead levels) following a dose of the chelating agent, penicillamine. In this study the hyperactive children chosen were without known psychosis or neurological disease. The etiology of their hyperactivity was unknown. Higher lead values were seen for both measures in hyperactive children as compared to the controls. A total of 52 percent of the hyperactive group had blood-lead levels of 25 micrograms per 100 milliliters or above while only 25 percent of the controls were in this range. Similarly, 62 percent of the hyperactive group excreted 81 micrograms of lead per liter or above while only 13 percent of controls were in this range. Although the differences in blood levels were small for the two groups (26.2 for hyperactives and 22.1 for controls), the urine lead values were 144 and 77, respectively. This supports the authors' contention that probably many of the children had eaten paint and dirt when they were younger and that much of the lead being stored in the bones was subsequently released by the penicillamine treatment. It was concluded by David (1974b) that there is an association between hyperactivity and raised lead levels and that a large body-lead burden may exact consequences that have been hitherto unrealized. Although this demonstrates a (statistical) association, no inferences of causality are justified. It may be that lead causes hyperactivity, hyperactivity causes lead ingestion, or some third factor (e.g., low social class) is the true predictor of both lead ingestion and hyperkinesis. Further research is necessary to determine which of these relationships is accurate.

In order to fully appreciate the significance of the effects of lead on the physical and mental functioning of children, the magnitude of the problem must be recognized. Knowledge of the mechanisms and toxicity of lead in children must ultimately be applied to populations in terms of preventive and rehabilitative care. To address these issues, the descriptive epidemiology of lead poisoning in children and population based intervention programs will be discussed.

6.4.2 Scope of Problem of Childhood Lead Poisoning

According to McFeatters (1976), the U. S. Department of Housing and Urban Development estimates at least 600,000 U.S. children have high levels of lead in their blood. In 1971, a U.S. Public Health Service survey in 27 cities showed 21 percent of inner-city children had symptoms of lead poisoning. The National Committee for the Prevention of Childhood Lead Poisoning believes as many as 2.9 million American children run the risk of lead poisoning.

Accurate blood-lead determinations should provide the basis of any mass screening for childhood lead intoxication (American Academy of Pediatrics, 1969). Pending improvements in the analysis of lead in blood, the urinary ALA test and the analyses of lead in hair offer the best substitutes for the purpose of mass screening. Early detection efforts should be directed at children 12 to 18 months of age. Each abnormal test calls for thorough clinical evaluation of the patient and, at the very least, a confirmatory blood-lead determination.

In the absence of mass screening programs for lead poisoning itself, early recognition relies on identifying the child with pica. Suspicion of lead poisoning and indications for blood-lead analysis and other laboratory tests include: (1) pica in the child by history or observation either in the clinic or house; (2) symptoms of plumbism; (3) nutritional anemia, especially after 12 months of age; (4) aberrant behavior; (5) developmental delay, especially in speech development. Parental attributes which increase the risk of lead poisoning in the child include: (1) a working mother who does not monitor her toddler's activities during her absence; (2) the arrival of a newborn infant and possible lack of attention to the toddler; (3) a depressed, psychotic, or alcoholic mother; and (4) a history of pica in the mother or previous children of the mother.

Childhood plumbism in the United States is largely a disease of the big cities and especially of the inner-city areas where old deteriorated housing prevails. The interior woodwork, painted plaster, and wallpaper of houses built prior to 1940 may contain layers of flaking lead-pigment paints which have never been removed. Several such flakes may contain far more than the average daily intake of lead. Thus, children with a history of pica are likely candidates for lead poisoning. In New York City, lead poisoning in children used to result in deaths in about 15 to 20 percent of cases, and to neurologic and mental disturbances from encephalopathy in over 25 percent of cases. As shown in Table 6.23, of the more than 61,000 poisonings reported to the New York City Poison Control Center between 1954 and 1964, 3 percent or approximately 1,700 cases were due to lead (Jacobziner, 1966; Lutz, et al., 1970), and 128 of these were fatal. The apparent increased incidence of lead poisoning (comparison of 1964 with 1954) is believed due to the vigorous case-finding program, resulting in the discovery of cases in the asymptomatic state prior to onset of encephalopathy. The sharp decrease in the number of deaths in recent years in encouraging.

Jacobziner (1966) found that 54 percent of all deaths from lead poisoning occurred in 2-year-old children. Lead encephalopathy is encountered much

Table 6.23 CASES OF CHILDHOOD LEAD POISONING PLUS FATALITIES IN NEW YORK CITY FROM 1954 to 1964[a]

Year	Cases	Deaths	Case Fatality[b]
1954	80	12	15.0
1955	115	18	15.7
1956	99	9	9.1
1957	85	9	10.6
1958	116	21	18.1
1959	171	12	7.0
1960	146	18	12.3
1961	181	6	3.3
1962	198	9	4.5
1963	338	7	2.1
1964	509	7	1.4
Total	2,038	128	6.3

[a] Adapted from Jacobziner (1966) and Lutz et al., (1970).

[b] Deaths per 100 cases.

more frequently during the summer months but asymptomatic lead poisoning is a year-round disease. Forty-five percent of the total cases reported between 1954 and 1964 occurred between June and September, but the exact reason for this is not known.

6.4.3 Massive Intervention Programs

In Baltimore the child lead-poisoning problem was first recognized in 1931, and since 1935, the Health Department's Bureau of Laboratories had provided free blood-lead determinations to physicians and hospitals (Lutz, et al., 1970). In 1949 a public health nurse was appointed to investigate reported instances of abnormal lead ingestion by children and to correct the condition. In 1951, the city adopted legislation to prohibit the use of heavily-leaded paints for interiors of dwellings. No deaths from childhood lead poisoning occurred in 1965 and childhood lead poisoning cases dropped to 32, the lowest since 1952. The Baltimore experience shows that fatalities from lead can be reduced or prevented. Also, it demonstrates that in an effective campaign, the number of deaths should decline as the number of cases rise, if there is speed and efficiency of treatment.

The Chicago Board of Health in October, 1966, began a mass screening program using a blood-lead test to detect lead poisoning in children living in substandard conditions (Sachs, et al., 1970). Atomic absorption spectroscopy made it possible to screen 5,000 specimens in 1 month and to test a total of 68,744 children in 1967 and 1968 (see Table 6.24). Of the 68,744 children, 5.7 percent (3,935) had lead values of 50 micrograms per 100 grams of whole blood. Children with elevated lead values were referred to a special clinic established by the Chicago Board of Health for the diagnosis and treatment of lead poisoning. Twenty-nine percent of these referrals were treated with chelating agents and the remainder were screened periodically until their lead level returned to normal. There were no deaths from lead poisoning among the 68,744 tested in 1967 and 1968. The incidence of high-blood levels among children living in the same areas declined from 8.5 percent in 1967 to 3.8 percent in 1968. Blood-lead values were lowest in November through January and highest in June.

Guinee (1973) reports on a large screening program in New York City to detect elevated blood-lead levels in young children. In 1971, 100,000 children, age 1 to 6 years, were tested. Two percent of these children had blood levels of 60 micrograms or greater. Significantly elevated blood-lead levels were found three times more often among black children than among Puerto Rican children (see Figure 6.17). Seasonal variation of blood-lead levels again showed a summer peak which persisted when age and race were standardized. As would be expected, elevated blood-lead levels were usually attributable to the ingestion of chips of old lead paint found on the interior surfaces of deteriorating dwellings.

6.4.4 Sequellae of Excessive Childhood Lead Exposure

Albert, et al., (1974) assessed the nature and magnitude of the deleterious health effects of overexposure to lead in children. The study

Table 6.24 DATA OF SURVEY AREAS FOR CHICAGO BLOOD-LEAD SCREENING PROGRAM - 1967-1968[a]

Urban Area	A Number of Children Under 5 Years (1960 Census)	1967				1968				Totals for 1967-1968			
		B Number Tested[b]	Percent of A	Number With High Lead[c]	Percent of B	C Number Tested[b]	Percent of A	Number With High Lead[c]	Percent of C	D Number Tested[b]	Percent of A	Number With High Lead[c]	Percent of D
1	10,000	2,500	25	157	6.3	3,100	31	53	1.7	5,600	56	210	3.8
2	15,100	1,700	11	73	4.3	1,800	12	56	3.1	3,500	23	129	3.7
3	22,000	2,000	9	262	13.1	3,000	14	166	5.5	5,000	23	428	8.6
4	22,300	5,200	23	509	9.8	5,500	25	270	4.9	10,700	48	779	7.3
5	13,700	4,100	30	316	7.7	4,900	36	142	2.9	9,000	66	458	5.1
6	24,500	6,600	27	393	6.0	7,700	31	277	3.6	14,300	58	670	4.7
7	20,500	3,400	17	432	12.7	7,000	34	356	5.1	10,400	51	788	7.6
8	15,300	2,200	14	218	9.9	6,100	40	227	3.7	8,300	54	445	5.4
9	4,500	300	7	19	6.3	1,700	38	9	0.5	2,000	44	28	1.4
Totals	147,900[b]	28,000	19	2,379 =	8.5	40,800	28	1,556 =	3.8	68,800	47	3,935 =	5.7

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[a] Adapted from Lutz et al., (1970).

[b] Figures given to the nearest hundred.

[c] High lead equals 50 micrograms lead per 100 milliliters whole blood or higher.

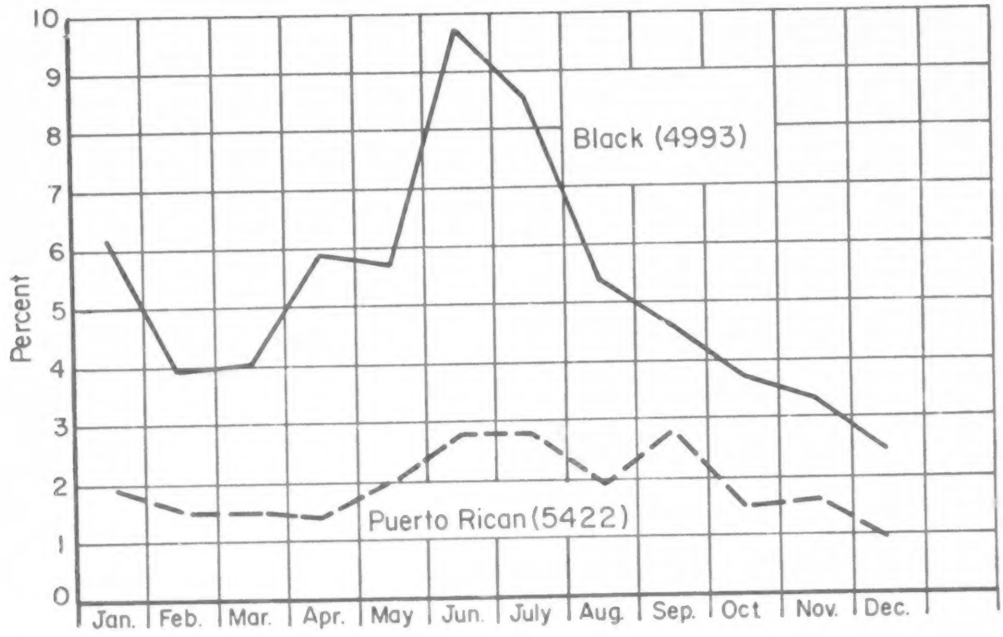

Figure 6.17 Percent of Black and Puerto Rican two-year old children with lead level of ≥ 60 μg/100 ml on first blood sample, by month, New York City, 1971. Adapted from Guinee (1973).

stemmed from concerns about the health of children in city slums who ingest leaded paint, but remain asymptomatic. The health implication of rising levels of lead in the environment from automotive emissions was also addressed. The study sample was derived mainly from a registry of children on whom blood-lead determinations had been made by the New York City Department of Health, supplemented by siblings of the registry cases and children from a lead belt area who had extractions of deciduous teeth in dental clinics. Information was obtained through parental interview, medical records, and psychometric evaluation. The data show that deleterious health effects occur both in children who were treated for severe lead poisoning and in children without diagnosed lead poisoning who had elevated blood-lead (equal or greater than 60 micrograms per 100 grams) levels. In the absence of diagnosed lead poisoning or elevated blood-lead levels, excess lead exposure, (measured in terms of high levels of lead in teeth) was not associated with deleterious health effects.

A screening and follow-up study on children with an increased lead burden was carried out by Pueschel, et al., (1972). In a house-to-house survey of an impoverished section of Boston, preschool children were studied for lead poisoning with the use of a simple and inexpensive screening procedure based upon the analysis of lead in hair by atomic absorption. Ninety-eight of 705 children screened in this fashion were found to have an increased lead burden. Chelation therapy was administered and environmental elimination of exposure to lead-containing substances was initiated. Fifty-eight children with an increased lead burden underwent comprehensive study and 1-1/2 years later reexamination took place: minor neurological dysfunction and various forms of motor impairment were observed in 22 percent to 27 percent of the children during each evaluation (Pueschel, 1974). Initial psychological assessment revealed low average mental abilities in the majority of children; 1-1/2 years later a significant increase in certain areas of intellectual functioning was noted.

6.4.5 Treatment Modalities

Chelation therapy has been cited by several investigators as the method of choice for returning blood-lead levels back to normal in cases (children or adult) of chronic or acute plumbism. The three chelating agents used to treat plumbism in the United States are edathamil calcium disodium (CaEDTA), 2,3-dimercaptopropanol (BAL) and d-penicillamine (PCA) (Chisolm, 1974). PCA is available in oral dosage form only (250-mg capsules) and is classified by the FDA as an investigational drug when used for lead poisoning. Equimolar amounts of these agents infused in rats under identical experimental conditions showed PCA to be appreciably inferior to CaEDTA and BAL in terms of the quantity of lead mobilized and excreted. Furthermore, a transitory increase in the lead content of some soft tissues was noted during mobilization with PCA, but not with CaEDTA or BAL. For all three drugs, the vast bulk of lead mobilized was derived from osseous tissue, presumably marrow, and the portion of lead loosely bound to bone. In children with acute symptomatic plumbism and in asymptomatic children with greater than 100 micrograms Pb per 100 milliliters of whole blood, combined BAL-CaEDTA at a maximum safe dosage is more effective than CaEDTA alone in terms of the amount and rapidity of diuresis of lead, reversal of metabolic abnormalities and, in critically ill patients, survival.

In adults with mild plumbism, parenteral CaEDTA is most effective, but oral PCA is superior to oral CaEDTA. Studies of children likewise show that CaEDTA administered intramuscularly evokes a considerably greater diuresis of lead than does oral PCA. The available data indicate that CaEDTA (or BAL-CaEDTA) should be used initially as the primary drugs. As a secondary drug, oral PCA is both adequate and much more convenient for long-term therapy when recurrent excessive intake can be controlled (Chisolm, 1974).

6.5 EPIDEMIOLOGY

A wide variety of epidemiologic studies have attempted to describe and quantify the health effects associated with lead exposure. The identification of especially susceptible segments of the population has also been a constant objective of these studies. Epidemiologic studies have been conducted in three general types of settings based on the characteristic levels of exposure: (1) studies of general populations in which lead exposure occurs at ambient conditions with no unusual sources of exposure (e.g., point sources or occupational). Inter-city comparisons are most representative of this type. (2) Intermediate level studies which examine populations selected on the basis of some unusual condition of exposure. Typically such persons are chronically exposed to ambient lead concentrations higher than those of the general population, yet substantially below industrial exposure levels. Persons residing in close proximity to freeways, working in dense vehicular traffic or living near smelters or other stationary sources of lead emissions are examples of "intermediate" exposure groups. (3) Studies of occupational groups exposed to air lead concentrations many times higher than general populations or "intermediate" groups; these groups represent the high extremes of the dose-response spectrum.

Attempts to establish a dose-response relationship between environmental lead concentrations and adverse health effects and/or the relative contribution of each of the various sources of exposure to body burden have met with only limited success. The underlying difficulty in such an analysis stems from the multiplicity of sources of lead exposure and the difficulty in accurately quantifying individual exposure.

6.5.1 General Populations

The risk to general populations from lead in air has become a matter of considerably concern (and the subject of many studies) in recent years. As Hammond (1977) has pointed out, studies of the fate of inhaled lead in man using conventional deposition and clearance measurements have not provided much useful information on the contribution of lead in ambient or industrial air to the internal dose at specified air lead concentrations. A more indirect but nonetheless useful approach to the problem proceeds from the assumption that the concentration of lead in the blood is proportional to the combined level of total uptake via many modes of exposure. It follows, then, that each environmental source (mainly air, food, and water) would contribute to the blood lead concentration in direct proportion to the total daily lead uptake. Although such a relationship has never been rigorously demonstrated, the studies discussed in this section, taken together, place the contribution of air lead to blood lead in the range of about 0.6-2.0 microgram/100 ml in blood per microgram lead/m^3 in air.

The earliest large-scale study of general populations was the "Three Cities Study" conducted in Los Angeles, Philadelphia, and Cincinnati, in the early 1960's (U.S. Department of Health, Education and Welfare, 1965). In addition to the general population, several groups whose exposure level is more representative of the "intermediate" exposure category (i.e., policemen, traffic controllers, garage employees, etc.) were also included as separate study groups.

The principal finding was that although significant differences in mean blood lead concentrations could not be found between the cities, persons who lived or worked in close vicinity of dense vehicular traffic such as traffic policemen, garage mechanics, and parking lot attendants had higher blood lead levels than others not similarly exposed. These data are shown in Table 6.25.

Goldsmith and Hexter (1967) calculated a logarithmic dose-response regression of blood lead concentrations from air levels. The data were mean blood lead levels and average estimated ambient air exposure from the cities included in the "Three Cities Study" (U.S. Dept. of Health, Education, and Welfare, 1965). Under the assumption that the major source of variation in ambient air lead was vehicular traffic, Goldsmith and Hexter calculated particle sizes and consequent retention rates on the basis of 50-80 percent (by weight) particles < 1.0 micrometer equivalent diameter. This is believed to be the characteristic particle size associated with automotive emissions. In general, ambient levels were measured by fixed samplers. Although it is recognized that they may not be truly representative of individual exposures, the authors felt they represented reasonable estimates of population averages. Goldsmith and Hexter concluded that a plotting of lead concentration in blood against lead concentration suggested a dose-response relationship. Data from four experimental subjects exposed to known, high concentrations of lead sesquioxide (Kehoe, 1966) are also plotted along the regression line to reinforce the validity of the relationship. The regression line itself was calculated only on the basis of the epidemiologic data, however. Figure 6.18 shows the regression line described by the equation:

$$\log \text{blood lead} = 1.265 + 0.2433 \log \text{atmospheric concentration}.$$

The contribution of air lead to blood lead, as inferred from the Goldsmith and Hexter (1967) regression, is about 1.3 microgram of lead per 100 ml of blood per 1 microgram of lead per m^3 in air.

The authors concluded that "the close correspondence between the experimental and epidemiologic data (obtained from Kehoe, 1966 and "Three Cities Study", respectively) make it seem likely that this relationship will be valid for a population having a dietary, beverage and cigarette smoking intake similar to that of American males".

Goldsmith and Hexter's proposed dose-response regression has been criticized on several grounds: (1) Ambient exposures were only estimates and were not necessarily measured at the same times and places at which the populations were exposed. Thus, air and blood levels even within the same exposure group (data points) are not related in any consistent, specific fashion. (2) The validity of calculating a regression line based on lead absorption from atmospheric lead has been challenged on the basis of the variable contribution of lead from other, more important sources of intake such as food and cigarettes, (National Academy of Sciences, 1972). (3) The

Table 6.25 BLOOD LEAD LEVELS OF SELECTED HUMAN POPULATIONS[a]

Type of Population	Mean Blood Lead, μg/100 ml	
Population without known occupational exposures:	Male	Females
Remote California mountain	12	9
Composite rural U.S.	16	10
Suburban Philadelphia	13	13
Composite Urban U.S.	21	16
Los Angeles aircraft workers	19	17
Pasadena city employees	19	12
Downtown Philadelphia	24	18
Population with known occupational exposures:		
Cincinnati policeman	25	
Cincinnati trafficman	30	
Cincinnati automobile test-lane inspectors	31	
Cincinnati garage workers	31	
Boston Sumner tunnel employees	30	

[a] Source: U. S. Department of Health, Education, and Welfare (1965).

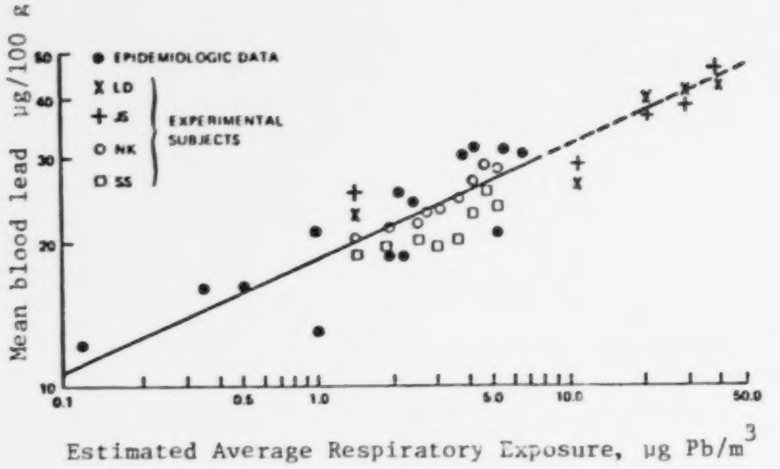

Figure 6.18 Mean blood lead concentration for epidemiologic and experimental respiratory exposures with regression from epidemiologic data only. Redrawn from Goldsmith and Hexter.
Source: National Academy of Sciences, (1972).

authors do not describe the methods of deriving their regression line nor do they present data on statistical tests of "goodness of fit" of the calculated regression line. (4) The methods used for deriving estimated "average" exposure levels for occupational groups (e.g., policemen, garage workers, and tunnel workers) are described only as a weighted average of presumed occupational and ambient exposure which were themselves estimated. (5) There are certain difficulties in interpreting findings, especially at the low end of the dose - response regression line. Lines representing confidence limits are hyperbolic and diverge markedly when applied to extrapolations at either end of the regression line; there is little validity to extrapolations beyond the range encompassed by actual observations. For a discussion on the matter of confidence limits calculated around a regression line see Goldwater (1972). The NAS report also comments on this phenomenon concluding the regression line cannot be applied with confidence to exposure conditions affecting the general population; this also applies to the general population of most large urban centers, inasmuch as average ambient air concentrations even in these centers do not generally exceed 2 micrograms per cubic meter.

In earlier studies such as the Three Cities Study, multiple uncontrolled variables associated with the various population groups have confused appraisal of actual integrated exposure and construction of the correct dose-response relationship. Because blood lead levels are determined by many factors in addition to respiratory absorption of lead in ambient air, the effects of these variables must either be controlled through statistical procedures or made as homogeneous as possible in the initial selection of the study subjects. Unless personal monitoring devices are used, one cannot establish the total integrated exposure over months or years for police officers, garage mechanics, "drivers", "commuters", aircraft workers or other similar groups. Occupational factors as well as variations in diurnal mobility patterns between individuals may markedly influence exposure level, yet these factors are not reflected in air sampling at fixed locations.

Tepper and Levin (1972) reported the findings of a survey of air and population lead levels in selected American communities, commonly referred to as the "Seven Cities Study". Among the cities surveyed were Cincinnati, Philadelphia, and Los Angeles, which had been extensively surveyed in 1961-1962 as part of the earlier "Three Cities Study". Also included were New York City, Metropolitan Washington (D.C.), Greater Chicago, Houston, and Los Alamos, New Mexico. These cities were selected on the basis of population density, level of industrialization and geographical location in order to represent a broad spectrum of these variables. The principal objective of the study was to evaluate the relationship between atmospheric lead levels and the concentrations of lead in blood of persons exposed to the atmospheres in question.

The Seven Cities Study focused particular attention on the definition of populations having a specific, consistent relationship to known air levels of lead. Unlike the Three Cities Study, populations sampled in the present study were women volunteers living within a prescribed distance (within a 1-mile radius) from the reference air sampling station. Moreover, the blood lead and air measurements were made concurrently. By confining the observations to members of one sex, requiring that the subject reside not more than 1 mile from the sampling apparatus, and eliminating as completely as possible extraneous, occupational lead exposures, the authors hoped to select a group which would accurately reflect absorption of ambient community atmospheric lead via the respiratory system.

In addition to the groups of women described above, husbands of 100 Los Alamos participants were also included as a separate study group.

Estimates of alimentary lead intake were obtained from measurement of the urine and feces of a subsample of 20 volunteers in each region. Each participant collected all excrement for a 10-day period. The principal findings were:

(1) Concerning changes in atmospheric levels of lead during the interval 1961-62 to 1968-69, the reported data demonstrate higher lead levels at most of the study sites during the more recent of the two periods. A careful examination of experimental methodology tends to exclude the possibility that this change is an artifact reflecting changes in technique.

(2) Since the F-ratio (testing the difference in blood lead levels among locations) was significant, individual comparisons were conducted between urban and suburban populations in the same metropolitan areas to examine whether or not blood lead levels reflect degree of urbanization for smokers and nonsmokers. In both smoking categories the Philadelphia urban groups were higher than the suburban; the Chicago urban groups were higher than the suburban and in New York the urban groups were also higher than the suburban. The probability of obtaining 6 relationships in this direction (urban > suburban) out of 6 comparisons is approximately equal to $1/2^6 = 1/64 = 0.015$, if one assumes either direction to be equally likely. Consequently, it appears that urban blood lead levels are higher than those from nearby suburban areas.

(3) Figure 6.19 presents mean blood lead levels and corresponding mean air lead levels at the sites where both were measured. The association between these mean values was measured by means of the Pearson Product Moment Correlation Coefficient and Kendall's Rank Correlation Coefficient. The values obtained were 0.412 and 0.354, respectively, for all data. Corresponding values for nonsmokers only were 0.400 and 0.345. The values were not significant at the 5 percent level. It was therefore concluded that there is no association between average blood and air lead concentrations.

(4) The observations that urban levels of blood lead are significantly higher than suburban levels, but that air concentrations of lead are not clearly reflected in blood lead levels generally, suggest that other variables are more important than ambient air lead levels in determining concentrations of lead in the blood. The precise nature of the variables, which evidently differ in the several regions studied,

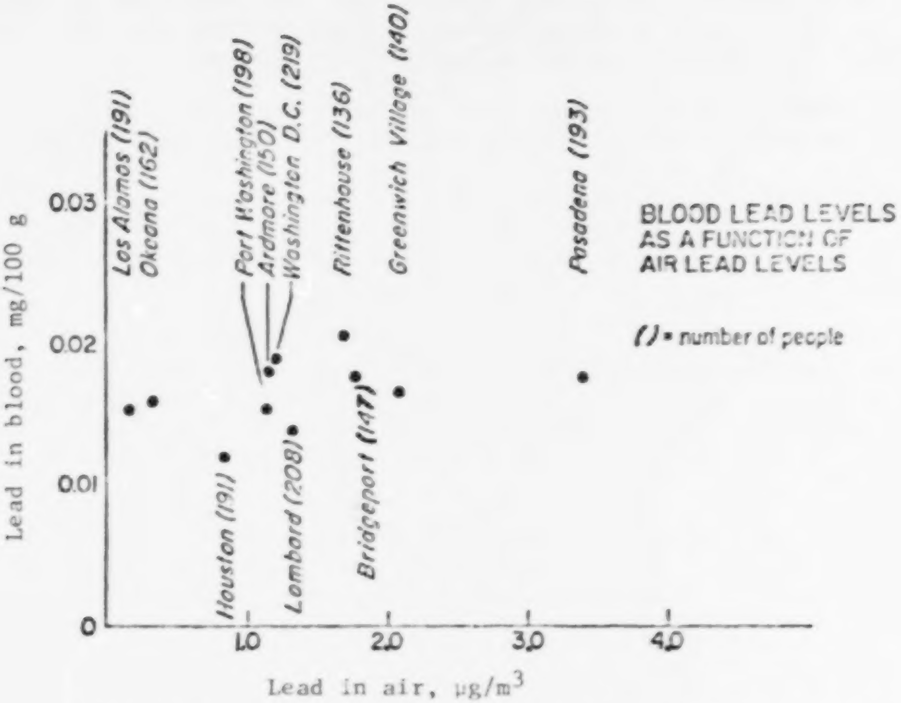

Figure 6.19 Blood lead levels and corresponding mean air-lead levels.
Source: Adapted from Tepper and Levin, 1972.

remains undefined. Presumably alimentary lead intake plays a significant role; however this was not clearly evident in the short-term metabolic study. Climatic factors may also be relevant.

(5) The analysis of fecal lead levels conducted to appraise alimentary lead intake, did not demonstrate high or low levels compensating for respiratory exposures so as to obscure effects of the latter.

(6) The relationship between age and blood lead level was examined by means of regression analysis and was found to be of no general significance.

(7) The influence of smoking upon blood lead levels was determined to be clearly significant. The blood lead level of smokers exceeded that of non-smokers and previous smokers. The relationship held true for males as well as females in the husband-wife pairs in Los Alamos.

(8) The examination of blood lead levels in husband-wife pairs in Los Alamos revealed a significant difference between males and females. The basis for this difference was not established. Probably, it cannot be attributed to occupational factors, for the work of each individual was characterized and conducted under comprehensive and detailed industrial hygiene supervision. Generally, men smoke more than do women; however, the blood lead in males remained higher than in female smokers and non-smokers.

Since men have generally higher hematocrit levels than women and since lead is transported in association with red blood cells, the possibility exists that higher blood lead concentrations in men reflect a higher level of circulating red cells.

Although both men and women of the studied Los Alamos couples consumed diets presumably similar in composition, the men consumed a generally greater quantity of food. It is therefore likely that the alimentary exposure of men to lead may be greater than that of women.

In summary, the Seven Cities Study failed to find a significant correlation between air lead and blood lead levels over an air lead range of 0.17-3.39 micrograms/m^3. Such a finding should not be unexpected, however, due to the narrow range of ambient conditions examined, the relatively small contribution to total intake (only about 20-30 percent) contributed by air at such low exposure levels, and the fact that the air data were obtained from fixed outdoor sampling stations which cannot estimate individual exposure levels precisely enough.

Azar, et al., (1975) examined the effects of air lead exposure indices of lead absorption such as blood lead, urine lead, D-ALA, (delta aminolevulinic acid) and ALAD (aminolevulinic acid dehydratase) activity. Personal air samplers were used to monitor the air lead exposure of 30 male subjects in each of 5 locations in the United States, 24 hours a day for periods ranging from 2-4 weeks. During this period, blood samples were obtained for blood lead and ALAD activity analyses and urine samples were analyzed for lead, D-ALA excretion, osmolarity and creatinine. Smoking data was obtained by means of a questionnaire. Two types of personal samplers were used to quantify level of airborne lead exposure. One type of unit was equipped with a cyclone device, which could separate respirable from non-respirable particles. These were used in the two taxicab studies. The second type was a Casella unit which was more portable, but since it did not have the cyclone device, only total air lead exposure was measurable.

The five sites were selected to represent a wide range of air lead exposures. Taxicab drivers were studied in Philadelphia and Los Angeles. Participants at Starke, Florida, Barksdale, Wisconsin and Los Angeles were thought to be representative of non-occupationally exposed groups.

The average exposure, urine and blood responses were computed for each subject in the study. Statistical analyses were based on these within subject averages. Site specific averages were computed based on individual averages at each site. These were subjected to an analysis of variance to determine whether there were significant differences between average urine and blood responses at the five sites. The relationship between air lead and the blood and urine responses were evaluated using regression techniques. Homogeneity of the slopes were checked by multiple regression techniques and the data were analysed in both natural physical units and logarithmic units (base 10 logarithms of the natural units). The logarithmic relationship gave the best fit to the data.

Table 6.26 shows air-lead exposure levels which were calculated by combining the work exposure ("on duty") with the home exposure ("off duty") on a time-weighted basis. When a cyclone device was used, the data are referred to as "Respirable" and when not used, as "Total". Exposures ranged from a low of 0.22 micrograms/m^3 at Starke to a high of 9.12 micrograms/m^3 obtained from a Los Angeles cab driver. Respirable air lead exposures were significantly less than total exposures, indicating that a significant quantity of the lead was contained in particles >10 microns in diameter which do not penetrate the lung. (These large particles could be swallowed, however.)

Despite air lead levels approaching 10 micrograms/m^3, only one individual in 150 had abnormal blood or urine levels. The source of exposure in this case was not lead from ambientair but rather from moonshine whiskey. (This subject was not included in subsequent analyses.) Statistical analysis of the site specific data showed that there was no significant correlation between air and blood lead at any of the five sites, indicating either (1) that there is in fact no correlation between air lead and blood lead, or (2) thirty subjects is too few to demonstrate significance, or (3) the range of data is too narrow to show significance, or (4) variables other than air lead (e.g., lead ingested from food and drink) are overwhelming any effect which air lead might have on blood lead. An analysis of the data for 149 of the subjects using a multiple regression technique indicated that variables other than air lead were affecting blood lead.

TABLE 6.26 MEAN SUBJECT AIR LEAD EXPOSURE[a]

Site	Lead Concentration, $\mu g/m^3$ ± 1 S.D.				
	On Duty		Off Duty	Combined Exposure	
	Total	Respirable	Total	Total	Respirable
Philadelphia, Pa Cab drivers	5.10 ± 1.11	4.34 ± .86	1.48 ± .23	2.62 ± .42	2.37 ± .34
Starke, Fla.	2.01 ± 2.52	1.39 ± 2.39	0.37 ± .31	0.81 ± .82	0.64 ± 0.78
Barksdale, Wisc.	2.84 ± 5.19	N.D.[b]	0.36 ± 0.14	1.01 ± 1.43	N.D.
Los Angeles, Calif. Cab drivers	9.42 ± .98	7.48 ± .92	4.22 ± 1.28	6.10 ± 1.02	5.37 ± 1.02
Los Angeles, Calif. Office workers	3.05 ± .76	N.D.	3.07 ± .81	3.06 ± .75	N.D.

[a] Source: Azar et al. Reprinted from Lead: Environmental Quality and Safety Supplement, Vol 2, T.B. Griffin, and J. H. Knelson (Eds.) (c) George Thiem Verlag, Stuttgart (1975).

[b] N.D. = Not determined.

Figure 6.20 shows that the data tended to clump into 5 subgroups by location. The average relationship between air lead exposure and blood lead concentration was obtained by drawing a line with a slope of 0.153 through the average blood lead concentration for 149 subjects. The resulting line was defined by the equation: log blood Pb = 1.2257 + 0.153 log air Pb. The slope of this regression was significantly ($p < 0.01$) different from zero (95 percent Confidence Limits, C. L. = ± 0.079). Approximately 56 percent of the variance in blood Pb is not explained by air Pb ($R^2 = 0.436$). Figure 6.20 also shows the regression lines obtained when the data from all sites are combined and adjusted to a common slope of 0.153. This is justified since the slopes are homogeneous. There was a significant correlation between log air lead level and log blood lead level after pooling data from all sites. The contribution of air lead to blood lead was found to be approximately 1.0 microgram of lead per 100 ml of blood per 1 microgram per m^3 of air over the range of air lead concentrations studied. This estimate is somewhat less than that estimated from Goldsmith and Hexter's (1967) equation (i.e., 1.0 vs. 1.3 microgram/100 ml for each 1 microgram lead in air, respectively).

The slope of this regression line (0.153) is less than that found by Goldsmith and Hexter (1967) and considerably less than that based on the theoretical calculations of the Environmental Protection Agency shown in Figure 6.22 as "EPA line".

Hammond (1977, personal communication) has applied the mathematical model described by Azar, et al., (1973) to empirical data published by Rabinowitz (1974); Griffin, et al., (1975); Fugas, et al., (1973); Prpic-Majik, et al., (1973); and Williams, et al., (1969) in order to compare actual data to predictions derived from the model.

The regression equation developed by Azar, et al., (1973; 1975) is as follows:

$$\log \text{PbB} = 1.226 + 0.153 \cdot \log \text{microgram Pb/m}^3$$

where

PbB = blood lead level
Pb/m^3 = air lead level.

This equation says, in effect, that for this particular population the average PbB at 1 microgram Pb/m^3 was:

$$\log \text{PbB} = 1.226 = 16.8 \text{ microgram/100 ml}$$

since the term ($0.153 \cdot \log \text{microgram Pb/m}^3$) reduces to zero when air Pb = 1 microgram/m^3.

For any other population under study, the constant for PbB at air lead = 1 microgram Pb/m^3 will be unique to that population and will depend upon all sources of lead intake. In order to solve for the constant describing log

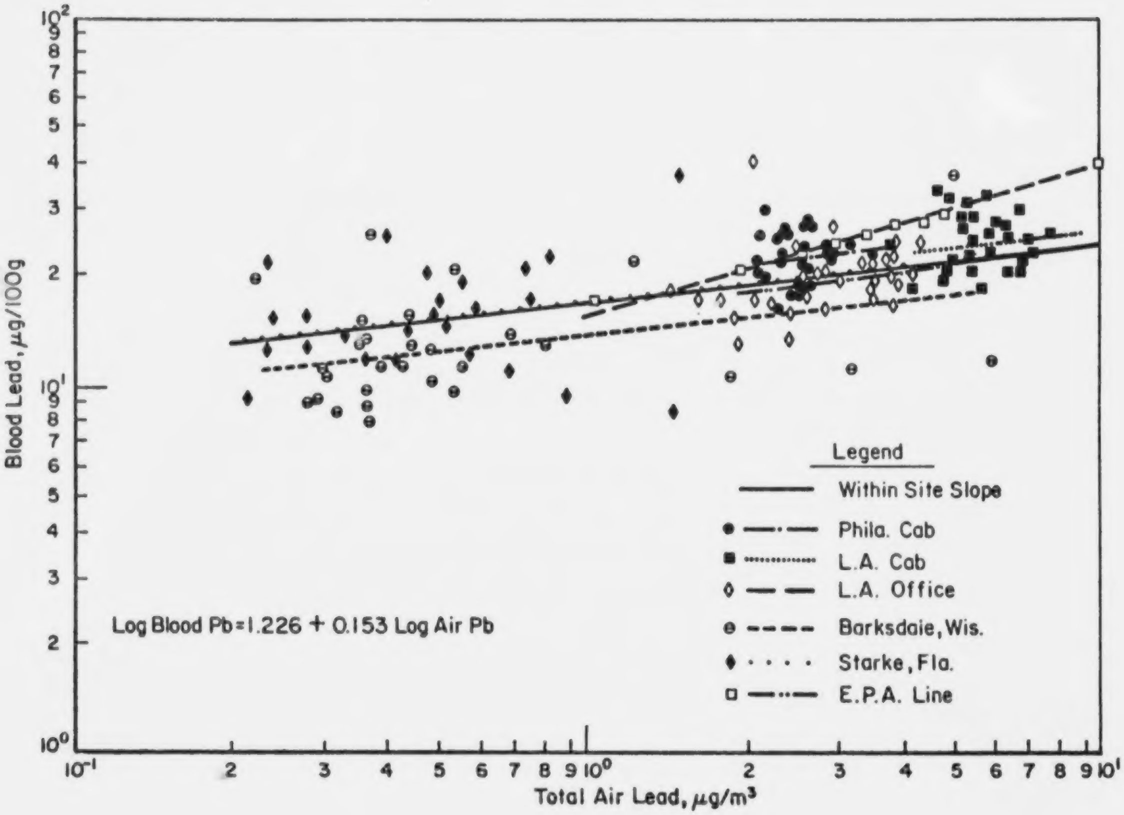

Figure 6.20 Blood lead versus total air lead

Source: Azar, et al. Reprinted from Lead: Environmental
Quality and Safety Supplement, Vol. 2.
T. B. Griffin and J. H. Knelson (Eds.)
(c) George Thiem Verlag, Stuttgart, 1975.

PbB at 1 microgram Pb/m^3, baseline PbB at a known small air lead concentration can be used. Taking an example, Coulston, et al., (1972) determined PbB in a group of men known to breathe air lead at 0.2 microgram/m^3 throughout the day. Solving for the term b in a = b + c,

a = log observed PbB
b = unknown constant
c = 0.153 · observed air lead, microgram Pb/m^3.

Using the Azar model, it is necessary to calculate a new constant for any particular group, log PbB at 1 microgram Pb/m^3. In Table 6.27 the baseline data for PbB at low, known air lead is given. Data for log Pb at 1 microgram Pb/m^3 are then calculated. This is the constant b described above.

Using the calculated constant for log PbB at 1 microgram Pb/m^3, the predicted PbB at the high air lead concentration is compared to the actual PbB measured. Finally, the contribution of air lead to PbB as actually observed is given.

Predictions are also provided for PbB's at several air lead concentrations breathed for 40 hours per week against a background PbB of 23.5 with an assumed nonoccupational air lead of 1 microgram/m^3.

It is evident from these data that the Azar model for regression of PbB on air lead predicts fairly accurately the group mean PbB's which have actually been observed among workers and human volunteers whose air lead exposures were fairly accurately known. It is also evident that as air lead increases, its impact on PbB, as designated in the last column of the table, becomes progressively smaller. Thus, excursions of air lead exposure over the suggested maximum of 100 microgram/m^3 would likely have only modest impact on the internal dose as reflected in PbB's. The physiological basis for such a phenomenon is not known.

Certain seeming discrepancies occur in Table 6.27. For example, an average air lead exposure of 27 microgram/m^3 (Prpic-Majic, 1973; Fugas, 1973) yields a predicted PbB of 46.8 while an average air lead exposure of 72.2 microgram/m^3 is predicted (last horizontal column) to yield a somewhat lesser PbB of 45.2. This discrepancy is due to the fact that in the former case PbB at 1 microgram/m^3 is 28.3 (antilog 1.4513) while in the latter case it is only 23.5. This only serves to highlight the fact that the impact of air lead on blood lead is very much dependent upon the background of non-air ources of lead.

It may be argued that the Azar model is invalid for industrial situations in which the particle size range and chemical composition of the lead aerosols may be quite different from those encountered in the general ambient air situation prevailing in the Azar study. Nevertheless, predicted values based on the Azar regression equation are quite consistent with the limited experimental data available concerning industrial exposure.

While all of the studies presented in this section have some objectionable features the estimates of the contribution of air lead to blood lead which

Table 6.27 THE IMPACT OF AIR LEAD ON BLOOD-LEAD LEVELS; A COMPARISON OF ACTUAL DATA TO PREDICTIONS USING MATHEMATICAL MODEL[a,b]

Baseline			"High" Air Exposure		PbB			
PbB at	μg/m³	log PbB at 1 μg Pb/m³	μg Pb/m³	log μg Pb/m³	Predicted	Actual	μg PbB/ μg/m³	Reference
11.2	0.2	1.1561	1.6	0.2041	15.4	12.9	1.2	Rabinowitz, 1974
21.8	0.2	1.4454	3.2	0.5051	33.3	27.6	1.9	Griffin, et al. 1975
20.1	0.2	1.4101	10.9	1.0374	37.1	36.4	1.5	Ditto
22.1	0.2	1.4513	35	1.5441	48.7	44.3	0.64	Fugas, et al., 1973 and Prpic-Majic, et al., 1973
22.1	0.2	1.4513	27	1.4314	46.8	42.9	0.78	Ditto
23.5	1.0	1.3711	51	1.7076	42.9	50.1	0.53	Williams, et al., 1969
23.5	1.0	1.3711	37	1.5682	40.8	39.7	0.45	Ditto
23.5	1.0	1.3711	33	1.5185	40.1	39.5	0.42	"
23.5[c]	1.0	1.3711	24.6	1.3909	38.4	--	--	
23.5[d]	1.0	1.3711	36.5	1.5623	40.7	--	--	
23.5[e]	1.0	1.3711	48.4	1.6848	42.5	--	--	
23.5[f]	1.0	1.3711	72.2	1.8585	45.2	--	--	

[a] Source: Hammond, P. B. (1977, personal communication).

[b] Azar, et al., 1973.

[c] Prediction assuming inhalation of 100 μg/m3 air lead 40h/wk. + 1 μg/m³ for remainder of week (128 h) (avg. = 24.6 μg/m³).

[d] Prediction assuming 150 μg/m³ 40h/wk. + 1 μg/m³ 128/wk. (avg. = 36.5 μg/m³).

[e] Prediction assuming 200 μg/m³ 40h/wk. + 1 μg/m³ 128/wk. (avg. = 48.4 μg/m³).

[f] Prediction assuming 300 μg/m³ 40h/wk. + 1 μg/m³ 128/wk. (avg. = 72.2 μg/m³).

they have provided are remarkably consistent. These estimates suggest that each microgram/m^3 of lead in air contributes approximately 0.6 to 2.0 microgram lead per 100 ml of blood. These data are also in agreement with estimates derived from occupational groups presented in Section 6.5.3.

6.5.2 Intermediate Levels of Exposure

Studies of persons regularly exposed to unusually high ambient lead concentrations (over 10 microgram/m^3 for all or part of the day) both from mobile and stationary sources have been much more successful than general population studies in demonstrating relationships between levels of lead in air and those in blood. Actually, it is only under these circumstances that respiratory intake of lead accounts for an appreciable percentage of total absorption. It should be mentioned that few of the persons in the intermediate category are exposed to sustained levels of over 10 microgram/m^3 for more than a few hours a day.

Chronic exposure to intermediate levels of lead from mobile sources may occur either as a result of residing in close proximity to high traffic density (i.e., freeways) or from occupations which involve exposure to above average amounts of automotive exhaust either indoors or outdoors. Policemen, taxi drivers, garage attendants and mechanics are the most common examples. Populations residing near stationary sources of lead emissions such as primary and secondary smelters and battery plants have also been studied. The effects of exposure to higher than average amounts of lead among the Wenatchee orchardists and their families have also been reported.

6.5.2.1 Mobile Emissions Sources--

Thomas, et al., (1967) attempted to determine whether persons living near freeways in Los Angeles County have increased levels of lead in blood. Fifty adults who had resided for at least 3 years within 76.2 meters (250 feet) of a freeway were compared with 50 who had resided for a like period near the ocean or at least 1.6 kilometers (1 mile) from a freeway. Average blood-lead levels were substantially higher in the population sample living near the freeway. However, blood-lead levels of these individuals were similar to other Los Angeles populations and lower than those reported for some other urban populations. The observed difference between the two population samples is consistent with the existence of coastal-inland atmospheric lead and blood-lead gradients within the Los Angeles Basin.

The effect of distance of residence from highways upon blood-lead levels among black females has been investigated (Daines, et al., 1972). Average annual air-lead levels on the front porches of homes located 3.7, 38.1, and 121.9 meters away from a highway were 4.60, 2.41, and 2.24 micrograms per cubic meter, respectively. There was no significant difference between the outside air-lead concentrations at 38 and 122 meters, but both were different from the air-lead concentration at 3.7 meters from the highway. This rapid nonlinear decrease in airborne lead with distance from the source has been observed for mobile as well as stationary lead sources. Concentrations of lead in dustfall also decrease rapidly with increasing distance from the source. Average annual air-lead levels in the front room of houses at the three sampling points also reflected this nonlinear decrease, being 2.3, 1.50, and 1.57 micrograms per cubic meter as the distances increased.

Average blood-lead levels in the study subjects were 23.1, 17.4, and 17.6 micrograms of lead per 100 grams at 3.7, 38.1, and 121.9 meters, respectively. The average blood-lead levels at the two more distant sampling sites differed significantly from the average at 3.7 meters, but did not differ significantly from each other.

Among the homes closest to the highway (3.7 meters), air-lead and blood-lead levels were significantly lower for subjects whose homes were air-conditioned than for similar subjects in homes without air-conditioning. Significant differences in air-lead, but not in blood-lead levels were observed for subjects in homes at 33.4 and 457 meters from a turnpike. The average outdoor air-lead levels at 33.4 meters and 457 meters were 1.95 and 1.73 micrograms per cubic meter; blood leads at these sites averaged 15.7 and 16.1 micrograms per 100 grams, respectively. In this experiment the air-lead levels, though statistically different, would not necessarily be reflected in higher blood-lead levels, because daily respiratory lead absorptions nearer the turnpike would only amount to about 1 microgram of lead per day more than at the distant site (U.S. Environmental Protection Agency, 1972).

Groups exposed to above-average amounts of automotive exhaust outdoors, such as policemen, may or may not have lead levels above those of comparable nonexposed groups according to a U.S. Environmental Protection Agency (1976) report. Differences, when present, are small (10 to 20 percent), but ranges are sometimes above normal limits. However, groups similarly exposed indoors (U.S. Dept. of Health, Education and Welfare, 1965; Tola, et al., 1972; Gothe, et al., 1973) such as parking garage employees, consistently have 20 to 40 percent higher levels than ordinary groups and a greater number of individuals with above-normal levels (blood lead of 40 microgram/100 ml or higher). Groups exposed in automotive repair facilities (U.S. Dept. of Health, Education and Welfare, 1965; Tola, et al., 1972) consistently have higher levels (20 to 100 percent higher) because exposure to solder, batteries, etc., is added to exposure to automotive exhaust. The range of levels is increased, and many are above 40 microgram Pb/100 g blood, as shown by the Three Cities Study.

Lawther, et al., (1972) studied airborne inorganic lead and its uptake by inhalation using three different types of data: (1) measurements of airborne concentrations of inorganic lead compounds taken in a busy London street and at a control site away from traffic, (2) measurements of the blood-lead concentrations in London taxi drivers using day workers as the test group and night workers as the controls; and (3) visual appearance of particles collected from the general atmosphere of London, from a busy London street and from the exhaust gases of petroleum and diesel engines.

Blood-lead and carboxyhemoglobin levels were studied among London taxi drivers on both the day and the night shift. Significant differences were found in blood carboxyhemoglobin, but not in blood-lead levels, when comparing smoking and non-smoking day-shift drivers to similar night-shift drivers. Lawther, et al., (1972) concluded that the day drivers had a greater exposure to motor car exhaust than the night-shift drivers because they had significantly higher blood carboxyhemoglobin levels and therefore "it would seem that little of the lead found in their blood is attributable to the lead they inhale while driving in London streets". Unfortunately, both differences in smoking intensity between smoking groups, as well as actual differences in air and dietary lead exposure could explain these results and neither was measured. Furthermore, information was not obtained regarding the exposure of the drivers when they were off duty (U.S. Environmental Protection Agency, 1972). Thus, the relative contribution of automotive exhaust versus other sources of lead remains unresolved.

Iwata, et al., (1971) described the effects of lead in auto exhaust on traffic controllers. The study measured lead in areas representative of the controller's work environment, along with medical examinations for signs of lead toxicity. Lead concentrations in air ranged from 3.3 micrograms per cubic meter to 9.6 micrograms per cubic meter. Medical examinations were carried out on 17 traffic controllers (Group I) and 14 indoor policemen (Group II). Subjective symptoms included headache and nettle rash, sore throat, nausea, constipation, lumbago, and dizziness. More complaints were found in Group I. No difference was found between the two groups in terms of whole blood specific gravity, amount of blood pigment, and punctate, basophilic erythrocyte level. A coproporphyrin test of the urine of one subject in Group I was positive. The average level of lead in urine ranged from 14.1 to 25.9 micrograms per liter in Group I and 10.4 to 26.2 micrograms per liter in Group II. The average level of lead in blood ranged from 12.3 to 24.5 micrograms/100 ml in Group I and 10.1 to 17.3 micrograms/100 ml in Group II, indicating slightly higher levels in Group I, however, these differences were not large enough to be statistically significant.

Landrigan, et al., (1975b) discovered three cases of mild lead poisoning among instructors at an indoor pistol range. These cases were characterized by blood-lead levels greater than 100 microgram/100 ml of blood, free erythrocyte protoporphyrin levels greater than 450 micrograms/100 ml of red blood cells, abdominal pain, and, in one instance, by slowing of motor and sensory nerve conduction velocity. Fragmentation of bullets during firing, explosive vaporization of primer, and aerosolization of lead suboxide particles during bullet molding appear to have been the major sources of airborne lead.

6.5.2.2 Stationary Emissions Sources--

Stationary sources of lead emissions can be divided into three categories:

(1) Primary smelters where ore is processed. Because lead ore generally will contain other metals (such as zinc, cadmium, bismuth, and arsenic), effects observed in exposure studies may not always be caused by lead alone.

(2) Secondary lead smelters and lead processing plants.

(3) Miscellaneous sources. These may include industrial processes where the main objective is not to obtain or process lead. An example is the recovery of copper from cables coated with polyvinyl chloride plastic, during which lead from the plastic may be released.

A recent Environmental Protection Agency report has summarized the studies which have examined the effects of lead exposure on persons residing near stationary lead emitting sources (U.S. Environmental Protection Agency, 1976). Extensive investigations of the effects of lead exposure on people living near primary smelters have been performed in El Paso, Texas; Helena Valley, Montana; Kellogg, Idaho,; and the Meza Valley in Yugoslavia. Highlights of each of these studies will be discussed briefly.

The smelter at El Paso, Texas, has been operating since the late 1800's and produces not only lead but also copper and zinc (Landrigan, et al., 1975a; Texas Morbidity and Mortality Weekly Report, 1973). In addition to these metals, cadmium and arsenic are known to be emitted. The estimated lead emissions were 292 metric tons in 1969; 511 tons in 1970; and 312 tons in 1971. These figures, however, are only for stack emissions; it is not known how much lead may have been emitted from fugitive emissions via ventilation, windows, etc.

The areas studied included the so-called Smeltertown Section, a residential area less than 183 meters (200 yards) west of the smelter as well as some nearby communities farther downwind known to be impacted by the smelter emissions. The concentrations of lead in air are presented in detail by The U.S. Environmental Protection Agency (1976) and in the published reports referred to above. Daily lead concentrations in Smeltertown in 1972 ranged from 0.49 to 75.0 micrograms/m^3. For 86 sampling days in 1972, the average level was 6.6 micrograms/m^3. Air lead levels fell off rapidly with distance, reaching background values at 4 to 5 km from the smelter. High concentrations of lead were found in the soil, being greatest in the area nearest the smelter (geometric mean 1791 ppm lead). High concentrations of lead in house dust were also found, ranging from 400 to 58,800 ppm.

Determinations of lead in blood showed that 70 percent of children 1 to 4 years old living nearest the smelter had concentrations $>$ 40 micrograms/100 ml; whereas high blood levels were not so common in older children and adults. Children with blood-lead levels of 40 micrograms/100 ml or above lived in homes where the geometric mean lead content of house dust was 6450 ppm compared to 2070 ppm for children with blood-lead levels under 40 micrograms/100 ml. Landrigan, et al., (1975a) concluded that the main factor causing elevated blood levels in these children was ingestion or inhalation of dust containing lead. Data on dietary intake of lead have not been obtained, but because the climate in El Paso and the nearness to the smelter prevents any farming in the area, it is probable that the lead intake via food for this study population does not differ markedly from other areas in El Paso (U.S. Environmental Protection Agency, 1976).

A smelting complex in East Helena, Montana, also has been investigated as a source of airborne lead pollution. Zinc, cadmium, and arsenic are known to be emitted in addition to lead. The precise quantity of lead emissions is not known (U.S. Environmental Protection Agency, 1976).

Air concentrations of lead were measured in 1969, and in East Helena the average concentration at several stations varied from 0.4 to 4 micrograms/m^3; the maximum 24-hour value was found to be 15 micrograms/m^3. In the further distant city of Helena, the average concentration was 0.1 microgram/m^3. Lead in soil was found to be 4000, 600, and 100 ppm at distances of 1.6, 3.2, and 6.4 km (1, 2, and 4 miles), respectively, from the smelting complex; whereas, in uncontaminated soil near the Helena Valley it was 16 ppm. Deposited lead (dustfall) was found to vary from 3 to 108 mg/m^2/month in East Helena; whereas, in Helena it varied from 1 to 7 mg/m^2/month.

Studies on humans were limited to children; lead in hair and blood were found to be higher in East Helena than in Helena. Averages were 15.6 and 11.6 micrograms/100 ml in blood and about 40 and 13 ppm in hair (Hammer, et al., 1972). Both blood lead and hair lead findings are suggestive of greater lead exposures near the smelter. The blood values indicate that lead absorption, although elevated near the source, was within normal limits. No adverse health effects on these children have been noted.

The U.S. Environmental Protection Agency (1976) reported preliminary data on air lead in the vicinity of a lead-zinc smelter at Kellogg, Idaho, which showed that during 6 months in 1971 the average concentration of lead in air was between 6 and 8 micrograms/m^3. Children from this area had a mean blood level of 20.9 micrograms/100 ml and a mean hair-lead level of about 100 ppm. Based on air lead determinations, the exposure seems to be about twice as high as in East Helena, which is supported by the finding that lead in hair was twice as high. This exposure resulted in about 5 micrograms/100 ml higher lead values in blood. Subsequent studies in Kellogg indicated that 22 percent of children 1 to 9 years of age living within 1 mile of the smelter had blood lead levels of 80 micrograms/100 ml or higher and that all but one child in this area had a blood-lead level of at least 40 micrograms/100 ml (Anon., 1974).

Another survey in the area showed elevated blood lead levels in a high percentage of children living as far as 4.02 km (2.5 miles) from the smelter. A possible explanation for the difference in the surveys is that the earlier study involved primarily fourth-grade boys, whereas the second included mainly younger children. Moreover, two different laboratories whose quantification techniques have never been compared were used for the analyses (U.S. Environmental Protection Agency, 1976).

At the 300-year-old "Mezica" lead-zinc mine in Yugoslavia, a smelting plant was constructed in 1896. This caused considerable lead contamination of the topographically closed, long valley of the Meza river. Consequently, for many generations inhabitants have had lifelong exposure to relatively high ambient lead. From 1968 a broad ecological and epidemiological study was conducted on a population composed mostly of women and children (Graovac-Leposavic, et al., 1973). The aims of this study were:

(1) To determine whether the population is unduly exposed to lead;
(2) To establish the level of the exposure in relation to the geographic location to the source of contamination;
(3) To discover the integrated lead exposure (lead body burden) from birth; and
(4) To find out by medical, biochemical and toxicologic methods any possible effects attributable to lead exposure.

For detailed study 286 persons were selected, together with 52 controls. Medical, biochemical, toxicological, hematological and genetic investigations were performed.

Many tests for evaluation of body burden were applied. The authors felt that determination of ALA represented the most suitable test. To establish integrated exposure, lead mobilization by CaEDTA injection was performed in 209 persons. It was established that lead body burden in exposed persons was up to 10 times higher than in unexposed controls.

Of 15 randomly selected persons, 13 showed some chromosome aberrations in the lymphocytes of the blood, which seems to be characteristic for lead effects. Applying the methods on the exposed population in the valley, it was not possible to reveal any express clinical signs of lead toxicity. The most significant changes were established in the enzyme system of porphyrin biosynthesis, chromosome aberrations and lead body burden.

It is clear from the preceding discussion that emissions from primary smelters may cause elevated blood levels and other signs of increased lead burdens in populations living near the emission sources. In El Paso and Kellogg, fairly high concentrations in blood of children in these areas were associated with increases in ALA excretion. Emissions from the El Paso smelter seem to have been of the same magnitude as those from the Meza smelter, but much higher air-lead concentrations have been found in Meza, probably as a result of different meteorological factors. Elevated lead levels in blood and urine and increases in ALA-U are, of course, results of lead exposure. Other reported symptoms, such as bone pains in Meza Valley, are probably not caused by lead. As pointed out earlier, primary lead smelters emit other metals, and nonspecific effects may well be caused by these or other contaminants (U.S. Environmental Protection Agency, 1976). Efforts should be made to separate effects of such contaminants from lead effects.

A recent EPA report (U.S. Environmental Protection Agency, 1976) investigated mortality patterns in counties containing primary smelters in comparison with contiguous, non-smelter counties to determine whether smelter emissions produced any noticeable health effects in terms of disease-specific mortality.

Several findings were consistent among all, or most of the sites examined. A majority of smelter counties showed an excess of deaths from 5 categories of deaths:

(1) All causes combined
(2) Cancer of the liver and biliary passages
(3) Cancer of the trachea, lung and bronchus
(4) Cancer of the kidney
(5) Cancer of the bladder.

Excesses from other (non-cancer) causes of death were frequently found in one or two of the smelter counties. These excesses were predominantly from respiratory diseases such as bronchitis, emphysema, asthma and pneumonia. Excess deaths from arteriosclerosis and small vessel disease were also seen in some smelter counties, however this pattern was not consistent.

These findings are interesting in view of the fact that traditionally, lead has not been thought to be a carcinogen in man, although it has been shown to induce cancer in rodents.

Two major faults emerge in this study, however. The first is the possibility that the effect is real (i.e., there is a genuine excess of cancer) but these effects might be attributable to factors other than lead. For instance, a variety of other carcinogens are known to be present in smelter emissions. Secondly, the study was unable to adjust for certain demographic factors which are independently associated with cancer risk (population, population density, income, race, education, and socioeconomic status). Therefore one has no assurance that smelter and non-smelter counties are comparable with respect to these factors. Findings from this study should be viewed with skepticism, however, this type of approach offers some possibilities if an adequate study design could be developed.

A good example of exposure from secondary smelters has recently been given by Nordman, et al., (1973). A random sample of 621 individuals 16 years old or older in an area near a secondary smelter in Finland was selected. Three hundred and thirty four individuals responded, of whom 41 were rejected for various reasons. Lead and ALAD in blood were determined in the remaining 293 individuals. The results were related to distance from the source and to dustfall levels of lead, which had been determined at 80 stations during a 1-month period. Significant negative correlations were found between distance from source and lead or ALAD in blood. This was especially pronounced in a group of women who spend most of their time at home. On a group basis, lead in blood was also found to be correlated to dustfall. However, blood-lead levels were generally below 30 micrograms/100 ml, and only in a group of males living in a zone where the dustfall was about 100 mg/m^2/month was the average 30 micrograms/100 ml. This dustfall is of the same magnitude as reported from East Helena.

Exposure from both a primary and secondary smelter in the inner city area of Omaha, Nebraska, has been reported (McIntire and Angle, 1972; Angle and McIntire, 1974). In the report, the authors did not take into account traffic density, but in a more recent study they concluded that elevated blood levels of lead could be related to proximity to a battery plant, traffic density, and substandard housing. (U.S. Environmental Protection Agency, 1976).

Martin (1974) reported an epidemiological survey of lead works of various types to determine possible adverse health effects on mothers and children living in the area. At a point approximately 100 meters from the factory chimney, average atmospheric lead concentrations of 3.0 micrograms/m^3 were found. Occasional 24-hour concentrations ranged up to a maximum of 28 micrograms/m^3. An extensive series of measurements of lead deposits was made in the vicinity and monthly figures of up to 392 micrograms/m^2 were found; environmental dusts contained concentrations of up to 5 percent, and soil concentrations ranged from 0.15 to 4.9 percent.

Initial results indicated that of 39 children under the age of 5 years living within 400 meters of the factory, 41 percent had blood levels of above 40 micrograms/100 ml whereas of 80 children living in the 400- to 500-meter range of the factory only 13.7 percent had blood-lead values above this level. Similarly, of 252 children attending local schools, 17 percent (44 children) were found with blood levels above 40 micrograms; 6 of these were over 60 micrograms. Of the 26 mothers living within the 400-meter range, 3 had blood-lead levels over 40 micrograms/100 ml, whereas of 53 living in the 400- to 500-meter range none exceeded this level. Three of the 4 children under school age with the highest blood leads, (75, 74, and 65 micrograms/100 ml), were living close to the works and 2 of these had fathers working there. In the third, the child's only known exposure to abnormal quantities of lead was the result of his proximity to the works. In the fourth, who lived in the 400- to 500-meter range, there was evidence of pica. Where raised blood levels were found, investigations were carried out in the home to exclude as far as possible sources of raised lead intake other than those derived from the factory. Apart from the occasional case of pica, no abnormal source was established. Thus, the principal cause of the raised levels was presumably emissions to the atmosphere from the factory, windborne dusts, or dusts from vehicles entering and leaving the works, or lead taken home on the person or clothing of a parent working in the factory, as described in Section 6.5.3.1.

Roberts, et al., (1974) report on the dispersal of lead and associated health effects of lead contamination near two secondary smelters located in different parts of Toronto. Each smokestack is about 100 meters south of a residential area and 100 to 200 meters north of an elevated expressway carrying 50,000 to 150,000 cars per day. Lead emissions from the two smelters were estimated at 15,000 to 30,000 kilograms per year. The high rate of lead fallout around the secondary lead smelters was attributed to episodal large-particulate emissions from low-level fugitive sources rather than from stack fumes. The lead content of dustfall, and consequently that of soil, vegetation, and outdoor dust, decreased exponentially with distance from the two smelters.

Blood samples were collected from 286 people close to the first smelter, 1425 people close to the second smelter and 1231 people in a similar socioeconomic urban control group. To determine the major source of increased lead absorption, blood and hair samples were obtained from 16 families living within 15 meters of the first smelter and 8 urban control families living in houses of similar age and upkeep. Lead content of potential sources of lead exposure in the smelter area and in the urban control group are shown in Table 6.28.

Between 13 and 30 percent of the children living in the contaminated areas had absorbed excessive amounts of lead (more than 40 micrograms/100 ml of blood and more than 100 micrograms/gram of hair) as compared with less than 1 percent in a control group. A relationship between blood and hair was established which indicated that the absorption was fairly constant for most children examined. It seemed that the ingestion of contaminated dirt and dusts rather than "paint pica" was the major route of lead intake. Metabolic changes were found in most of the 21 children selected from those with excessive lead absorption; 10 to 15 percent of this group showed subtle neurological dysfunctions and minor psychomotor abnormalities.

The total population of children under the age of 17 living in a working class area exposed to undue amounts of lead from lead smelter was examined in an investigation of the relationship between blood-lead levels, general intelligence, reading ability, and rate of behavioral disorder (Lansdown, et al., 1974). As shown in Tables 6.29 and 6.30, these investigators found that distance from the factory producing the lead pollution was related to blood-lead level and any measure of mental functioning. Lower levels of intelligence and higher rates of disturbance were attributed to social factors, rather than excessive lead exposure.

Both Roberts, et al., (1974) and Landrigan, et al., (1975a) showed that children living in close proximity of ore smelters have elevated blood lead concentrations. Also, both studies found that lead in soil, in dustfall and in the blood of children were strongly correlated with distance from the smelter stack.

In addition, Roberts, et al., (1974) linked their findings of behavioral abnormalities (hyperkinesis) among children hospitalized for excessive lead absorption with similar findings of David (1974a,b). Roberts, et al., however, do not define the clinical diagnostic criteria used to classify the children as hyperactive in their study. Thus, while there seems to be reason to suspect that there may be a relationship between elevated blood lead and hyperkinesis, inadequacy of study design and/or ill-defined criteria for diagnosing hyperactivity have been serious shortcomings of past studies. For this reason, many experts relegate these findings to unconfirmed reports requiring scientific documentation in future studies.

6.5.2.3 Miscellaneous Sources--

There have been very few epidemiologic studies of groups exposed to lead in which a large number of factors were documented and the results in

Table 6.28 LEAD ACCUMULATION BY PEOPLE LIVING CLOSE TO A SECONDARY SMELTER COMPARED TO AN URBAN CONTROL GROUP, AND SOME POTENTIAL SOURCES OF LEAD UPTAKE[a]

	Smelter Area			Urban Control Area		
Matrix Units	A.M.[b]	G.M.[c]	Range	A.M.	G.M.	Range
Blood (μg/100 ml)	31	27	12-61	19	17	8-40
Hair (μg/g)	52	41	14-166	17	13	3-39
Tap water (μg/liter)	6.8	5.9	2-14	1.40	1.3	1-2.4
Paint (percent by weight)	1.23	0.72	0.13-4.64	1.30	0.89	0.11-2.62
Dustfall (mg/m^2 per 30 days)	553	158	35-2334	25	23	17-36
Suspended particles (μg/m^3)	3.84	3.01	1-10	0.93	0.82	0.30-2.54
Outdoor dust (μg/g, D.W.[d])	5828	2416	578-39,500	1002	924	500-1561
House dust (μg/g, D.W.)	2055	1550	470-8400	845	713	351-2010
Garden soil (μg/g, D.W.)	2626	1715	355-8750	110	99	57-240
Vegetables, washed						
Lettuce leaf (μg/g, F.W.[e])	8.6	2.9	0.7-40	0.9	1.0	0.8-1.1
Radish tuber (μg/g, F.W.)	4.6	1.7	0.6-28	0.3	0.3	0.2-0.4
Tomato fruit (μg/g, F.W.)	0.33	0.32	0.25-0.40	0.24	0.23	0.10-0.30

[a] Source: Roberts, et al. Reprinted with permission from Science. (c) American Association for the Advancement of Science, 1974.

[b] Arithmetic mean.

[c] Geometric mean.

[d] Dry weight.

[e] Fresh weight.

Table 6.29 BLOOD-LEAD LEVELS IN SCHOOL-AGE CHILDREN AS A FUNCTION OF THEIR ADDRESS[a,b]

Distance from Factory, m	Number	Blood-Lead, μg/100 ml Mean	S.D.	Range
0-100	3	40	15	28-57
100-200	27	37	12	22-65
200-300	58	32	8	18-60
300-400	88	32	5	23-45
400-500	30	10	10	15-63

[a] Source: Landsdown, et al. Reprinted, with permission, from Lancet. (c) The Lancet, Ltd. (1974).

[b] Correlation between address and lead level: $r = 0.176$ ($P<0.05$).

Table 6.30 INTELLIGENCE AND BEHAVIOUR IN SCHOOL-AGE CHILDREN AS A FUNCTION OF THEIR ADDRESS DURING THEIR FIRST TWO YEARS OF LIFE[a,b,c]

Distance from Factory, m	Number	Mean I.Q.	Percent Disturbed	Percent Hyperactive
0-200	17	107	0	6.6
200-300	33	101	15.6	37.5
300-400	27	106	22.2	26.9
400-500	6	110	0	16.6
500+	138	96	30.1	40.0

[a] Source: Landsdown, et al. Reprinted, with permission, from Lancet, Ltd. (1974).

[b] Comparison between children within 500 meters of the dump and those at 500 meters or more:
I.Q.: $t = 4.057$ ($P<0.01$)
Disturbance: $\chi^2 = 9.4$ ($P<0.01$)
Hyperactivity: $\chi^2 = 3.3$ ($P>0.05$).

[c] All but 14.5 percent of the sample spent their first 2 years at the same address.

different exposure groups compared. One of the earliest of such studies concerned the orchardists in the Wenatchee area of Washington state who were exposed to lead arsenate,reported by Neal, et al., (1941) and followed up in a later study by Nelson, et al., (1973).

The lead concentrations observed were not as high as those sometimes seen in other industrial exposures, but that makes them particularly important because urinary lead levels ranged from slightly higher than that commonly found in urban communities up to levels typically seen among workers having moderate lead exposures in industry.

Among the factors studied in assessing the health of the orchardists were weight, blood pressure, diseases of the cardiovascular system, skin disorders, eye irritation, chronic nervous diseases, blood dyscrasias, kidney disease, pulmonary tuberculosis, visual acuity, syphilis, neoplastic disease, and fertility. Insofar as comparative data for other populations were available, no evidence was found that incidence of any of these conditions was altered by the exposure. Special attention was given to the medical examination of children because in the Wenatchee area, orchards surrounded the communities or the houses in which they lived. Consequently, there were unusual opportunities for children to be exposed to lead arsenate insecticide sprays and spray residues on branches, leaves, and grass, in addition to residues ingested on apples. In only one respect did these children differ from children in other districts: their urinary lead and arsenic concentrations were nearly twice as high as those of a group of 18 children measured at the same time in Washington, D.C. (who had a mean urine lead content of 0.026 milligram per liter; standard deviation, 0.0128). In reviewing this study, National Academy of Sciences (1972) concluded that there was no indication of adverse effects of lead arsenate exposure on the health of the Wenatchee children.

A follow-up study of this population was undertaken in 1968 (Nelson, et al., 1973). Over 97 percent of the original participants were successfully traced. There was an attrition of 452 by death among the 1231 original subjects. The overall mortality rate proved to be less than average for the area. There was also no correlation with exposure to lead and mortality.

6.5.3 Occupational Exposures

Occupational lead exposures represent the high end of the dose-response spectrum; it is among workers who mine, smelt, refine, and manufacture lead-containing or lead-painted products that the highest and most prolonged lead exposures are seen. Consequently, the study of occupational groups provides valuable maximal human health effects both in terms of high concentration and chronicity of exposure.

The clinical pattern of occupational lead intoxication has changed during the 20th century in that the incidence and severity of poisoning has decreased substantially in recent years. Whereas acute and occasionally fatal lead poisoning was seen early in the 20th century, today's cases are frequently diagnosed at an earlier, asymptomatic stage on the basis of abnormalties of biochemical, neurological, or renal function. Nevertheless, excessive lead absorption and its attendant health effects remain a serious and prevalent occupational hazard in the lead industries today. The findings of several recent surveys reported in this section indicate that present standards and work practices of the lead industry do not adequately protect lead workers from adverse health effects.

6.5.3.1 Recent Field Investigations--

Epidemiologic-studies conducted between 1975 and 1976 in five different lead facilities across the United States have shown unacceptably high blood lead levels and symptoms of lead poisoning in every plant studied (Center for Disease Control, 1977). The sites investigated included four secondary smelters and one lead chemicals plant (Eagle-Picher Industries, Joplin, Missouri), which produces such lead compounds as lead oxides, lead peroxide, lead sulfate, and lead silicate.

Information concerning the plants included in the investigation is given in Table 6.31. Hematologic, neurologic and renal damage due to lead were consistently reported. Inappropriate medical management (misuse of chelating drugs) and poisoning of worker's children from home contamination with lead dust were also observed in one or more of the plants.

Investigations at the Memphis, Tennessee, secondary lead smelter were prompted by reports of excessive blood-lead levels and clinical lead poisoning at this plant. Ninety-two percent of current employees and one former employee were examined, revealing blood-lead levels up to 184 micrograms/100 ml. Sixty-seven percent of the workers had blood lead concentrations above the currently proposed occupational standard of 60 micrograms/100 ml. Table 6.32 summarizes the distribution of blood-lead levels at the Memphis facility as well as from the other four sites. The highest levels were seen in production area workers, many of whom exhibited the following classical signs of lead poisoning:

Abdominal pain (17 percent)
Gastrointestinal dysfunction (22 percent)
Joint pain (28 percent)
Neuromuscular symptoms (27 percent)
Anorexia (23 percent)
Lead neuropathy (8.5 percent) weakness of wrist extensor muscles
Anemia (13 percent) defined by hemoglobin $\leq$ 60 microgram/100 ml.

Three workers were anemic; neurological symptoms including wrist weakness, ankle drop and tremors were noted in a few workers. Symptoms compatible with lead poisoning were noted in 38 percent of the 53 workers examined.

The most notable finding at this plant was the high incidence of renal function abnormality. Thirty-two percent of the workers had elevated blood urea nitrogen (BUN $\geq$ 20 mg/100 ml). Further studies revealed significant impairment of renal tubular and glomerular function in 7 workers which may represent early stages of lead nephropathy.

Table 6.31 DESCRIPTIONS OF LEAD PLANTS INVESTIGATED, 1975-1976[a]

Date of Study	Location	Type of Plant	Date Plant Began Lead Processing	Pounds of Lead Processed per Month
November 1975	Memphis, Tenn.	Secondary smelter	1948	2.3 million
March 1976	Joplin, Missouri	Lead chemicals plant	--	--
May 1976	Eagan, Minnesota	Secondary smelter	1948	1.5 million
January 1976	Salt Lake City, Utah	Secondary smelter	1975	30,000-250,000
March 1976	Atlanta, Georgia	Secondary smelter	--	--

[a] Source: Center for Disease Control, 1977.

Table 6.32 BLOOD LEAD LEVELS IN LEAD PLANT WORKERS[a]

Blood Lead Level µg/100 ml	Number of Workers in Each Group, Percent					
	Memphis, Tenn.	Joplin, Mo.	Atlanta, Ga.	Salt Lake City, Utah	Eagan, Minn.	Total
< 40	14(18%)	1(2%)	6(15%)	1(3%)	3(8%)	25(11%)
40 - 59	12(15%)	7(17%)	6(15%)	5(17%)	6(16%)	36(16%)
60 - 79	26(33%)	21(50%)	17(44%)	2(7%)	17(45%)	83(37%)
≥ 80	26(33%)	13(31%)	10(26%)	21(72%)	12(32%)	82(36%)
Total tested	78	42	39	29	38	226

[a] Source: Center for Disease Control (1977).

Investigations at the secondary lead smelter at Salt Lake City, Utah, revealed unequivocal lead poisoning in 52 percent of those examined; two hospitalized workers had blood lead levels over 250 micrograms/100 ml. In addition, 36 percent of the workers were anemic. These cases of acute lead poisoning were related to a change in process involving the conversion of two small rotary furnaces previously used to process antimony to lead processing. Inadequate ventilation was felt to be responsible for the elevated air lead levels in the plant.

The median blood lead level of 38 workers at the secondary lead smelter at Eagan, Minnesota, was 72.5 microgram/100 ml. Seventy-six percent had levels $\geq$ 60 microgram/100 ml. Weakness of wrist and/or ankle extensor muscles was seen in 10.5 percent of the workers; 26 percent had tremor of the outstretched hands.

At the Atlanta, Georgia, secondary lead smelter, 70 percent of the plants' 39 employees had blood lead levels $\geq$ 60 microgram/100 ml. The percentage of workers with blood lead levels $\geq$ 80 microgram/100 ml varied between 43 percent in January, 1975 (when a lead exposure problem was first identified) to 26 percent in February 1976. Workers at this plant who were treated with intravenous chelation were permitted to remain on the job during therapy, a practice condemned by the medical profession.

An important finding of the overall study was that blood lead and erythrocyte protoporphyrin (EP) were well correlated with symptoms of lead toxicity. Persons reporting symptoms during the year previous to testing had significantly higher blood lead levels than those without symptoms. Erythrocyte protoporphyrin (EP) levels were also well correlated ($r = 0.76$) with zinc protoprophyrin levels. Furthermore, the higher the blood lead or EP level, the greater the proportion of symptomatic workers. This correlation was better in circumstances where the duration of exposure was relatively short as in the Memphis facility (average duration of employment was 5 months) than in plants where the average duration of exposure was longer. In Eagan, Minnesota, and Joplin, Missouri, the average duration of exposure was 4 and 20 years, respectively. These data are shown in Table 6.33.

Forty-nine percent of workers with blood lead levels from 60-79 micrograms/100 ml reported symptoms consistent with lead poisoning during the year preceding examination. Twenty-three percent of workers with blood lead levels from 60-79 micrograms/100 ml were experiencing symptoms at the time of the examination. Since many of the symptoms reported were nonspecific, (i.e., headaches, joint pain, constipation) a similar questionnaire was administered to a control group composed on local workers having no known occupational lead exposure. The prevalence of reported symptoms consistent with lead toxicity was much lower among unexposed workers than among lead workers.

Anemia, defined by hemoglobin levels < 14 g/100 ml, was noted in 14 percent of workers at the Memphis plant and 31 percent at the Salt Lake City facility. The clinical significance of anemia depends upon the degree of hemoglobin depression, however, classical symptoms of anemia (i.e.,

Table 6.33 PERCENTAGE OF WORKERS WITH SYMPTOMS OF LEAD POISONING BY BLOOD LEAD AND ERYTHROCYTE PROTOPORPHYRIN LEVEL AT THREE LEAD PLANTS[a,b]

Location	Ratio, Percent of Symptomatic Workers by Blood Lead Level (μg/100 ml)			
	<40	40-59	60-79	>80
Tennessee	1/13 (8)	2/12 (17)	7/26 (27)	18/26 (69)
Missouri	[0/1 (8)][c]	4/7 (57)	7/21 (33)	7/13 (54)
Minnesota	[0/2 (0)]	2/6 (33)	9/14 (64)	5/12 (42)
	Erythrocyte Protoporphyrin Level, μg/100 ml			
	<100	100-199	200-299	>300
Tennessee	2/26 (8)	2/13 (15)	11/16 (69)	13/21 (62)
Missouri	[1/1 (100)]	4/10 (40)	10/15 (62)	9/15 (60)
Minnesota	[0/2 (0)]	1/5 (20)	[0/4 (0)]	15/23 (65)

[a] Source: Adapted from Center for Disease Control (1977).

[b] Two or more of symptoms of lead poisoning during past year.

[c] [ ] = 5 members or less.

tiredness, fatigue, etc.) are not generally seen until hemoglobin decreases below 8 g/100 ml. Decrement in work performance has been documented at hemoglobin levels of 11-13 g/100 ml according to the authors (Center for Disease Control, 1977). A dose-response effect between hemoglobin level and work performance was noted throughout the range of hemoglobin levels from 3-17 g/100 ml and no threshold effect was observed. Resistance to infection is also depressed in anemic persons although no precise information regarding the magnitude or threshold level for this effect is available.

Manifestations of lead toxicity also varied with duration of exposure. After brief exposure, (2-3 months) gastrointestinal sysmptoms predominated whereas constitutional symptoms and joint pains were relatively more common after prolonged exposure (over 1 year). Also, conditions of acute exposure lead to relatively more gastrointestinal symptoms than chronically exposed workers. Highest rates of gastrointestinal symptoms were noted in lead poisoning cases in Salt Lake City (3-4 months duration) while workers chronically exposed in the Eagan, Minnesota, plant exhibited more nonspecific, constitutional symptoms such as tiredness, weakness, irritability, and joint pain (Tables 6.34 and 6.35).

The relationship between duration of exposure to lead and manifestations is summarized below.

(1) Anemia - With one exception, anemia was observed only after two or more months of exposure.

(2) Neuropathy - Several workers showed wrist extensor or ankle weakness after 2-7 months of exposure. The lowest blood lead level associated with neuropathy was 78 micrograms/100 ml; most neuropathy cases had blood lead levels above 80 micrograms/100 ml.

(3) Nephropathy - No definite relationships were noted between duration of exposure and development of overt lead nephropathy. Some abnormalities of renal function were correlated with duration of lead exposure. At the Missouri plant, 32 percent of workers tested had elevated blood urea nitrogen (BUN). These workers had worked at the plant for 45-31 years. Eight percent of the Tennessee workers had elevated BUN levels and 8 percent of the Minnesota workers had elevated serum creatinine levels. With the exception of 3 workers who were all exposed to lead less than 2 months, no worker with less than 3-1/2 years of exposure had abnormal renal functions tests.

A survey of 228 children living in the area surrounding the Memphis, Tennessee smelter showed no excessive lead absorption, however young children of smelter workers were found to have elevated blood lead levels and 8 were hospitalized and treated for lead poisoning. Examination of 31 children (ages 1-9) at the Eagan, Minnesota plant revealed blood lead levels $\geq$ 30 micrograms/100 ml in 16 percent of the children, indicating increased lead absorption.

Table 6.34 FREQUENCY OF SYMPTOMS AMONG 22 CASES OF LEAD POISONING, UTAH, 1976[a]

Symptom	Number	Percent
Abdominal cramps	19	86
Nausea	18	82
Diarrhea	12	55
Headache	12	55
Dizziness	12	55
Anorexia	12	55
Vomiting	9	41
Paresthesias	9	41
Constipation	8	36
Fatiguability	8	36
Myalgias	7	32
Weight loss	6	27
Irritability	5	23
Chest pain	5	23
Muscle weakness	4	18
Tremor	4	18
Joint pains	4	18

[a] Source: Adapted from Center for Disease Control (1977).

Table 6.35 OCCURRENCE OF SYMPTOMS IN LEAD SMELTING PLANT EMPLOYEES, MINNESOTA, 1976[a]

Symptoms	Number with Sympton	Percent With Symptom
Tiredness	17	52
Loose bowel movements	11	33
Irritability	9	27
Joint pains	9	27
Muscle weakness	9	27
Loss of appetite	7	21
Headache	6	18
Leg cramps	6	18
Constipation	6	18
Nausea[b]	5	16
Trouble sleeping	4	12
Vomiting[b]	4	13
Abdominal pain	3	9
Weight loss[c]	2	6
Shakes	2	6

[a] Source: Adapted from Center for Disease Control (1977).

[b] Excluding 1 employee with symptom due to ulcers.

[c] Excluding 2 employees with symptom due to diet. Of the 2 with weight loss not related to diet, 1 lost 20 pounds in 15 months and 1 lost 22 pounds in 7 months.

Based on findings presented in the previous discussion, it is obvious that the currently accepted upper limit of a safe blood lead level (80 micrograms/100 ml) does not provide adequate protection against lead toxicity. If lead toxicity is to be prevented, the biologic monitoring system must remove the worker from exposure prior to the onset of illness. Clearly the present 80 micrograms/100 ml level does not provide adequate protection since anemia and other overt symptoms of lead intoxication were observed at blood lead levels below 80 micrograms/100 ml.

In the five facilities investigated, no workers showing evidence of lead related anemia, wrist weakness or lead related renal disease were associated with a blood lead level $< 60 \mu g/100$ ml. In fact, very few workers with blood lead levels $<$ 60 micrograms/100 ml had any symptoms consistent with lead intoxication. The authors concluded that the data in the report clearly support the setting of a biologic threshold limit value of 60 micrograms/100 ml for occupationally exposed populations and furthermore that this value should be revised downward in the event that deleterious health effects at blood lead levels $<$ 60 micrograms/100 ml can be demonstrated in the future (Center for Disease Control, 1977).

6.5.3.2 Dose-Response Relationships: Air and Blood--

Preliminary findings of a study by National Institute for Occupational Safety and Health (NIOSH) at the General Motors Corp. Delco-Remy battery plant in Muncie, Indiana, provide new information on the relationship between air and blood-lead levels (Wall Street Journal, 1977). NIOSH analyzed the data on lead levels in the blood of about 500 plant workers as well as the lead level in the air. Investigators found that the plant kept lead levels in the blood of over 90 percent of its workers at 60 micrograms/100 ml or lower by maintaining air exposures at a maximum of about 100 micrograms/m^3 in most work areas.

The studies of Williams, et al., (1969) and Williams (1972) cited in The OSHA Proposed Occupational Exposure Standard (U.S. Department of Labor, 1975) may be used to estimate the potential contribution of lead in air to blood lead levels. The air exposure data used by Williams, et al., (1969) was based on measurements obtained from workers in various departments of a storage battery factory who wore personal samplers for a full work shift for 2 weeks. Considerable variations were found both among departments and among individual personal samples. The study presents a correlation between the mean blood lead level, together with the upper and lower ranges, with air lead levels. In order to provide a maximum blood lead value of 60 micrograms/100 ml, the mean blood lead level in a population of workers must be maintained at about 40 micrograms/100 ml since a mean of about 40 micrograms/100 ml will result in a range in workers of approximately 20 micrograms at the lower limits to 60 micrograms at the upper limits. The Williams data suggest that air lead levels of 200 micrograms/m^3 correspond to a range of 48-92 micrograms/100 ml of lead in blood with a mean level of 70 micrograms/100 ml (84 micrograms/100 ml $\cong$ 80 micrograms/100 g). Similarly, air lead levels of 150 micrograms/m^3 correspond to a range of 38-82 micrograms/100 ml with a mean blood lead level of 60 micrograms/100 ml. It is apparent, therefore, that airborne lead levels of 200 or 150 micrograms/m^3 would result in unacceptable blood lead levels, i.e., greater than 60 micrograms/100 ml, for a significant number of employees (U.S. Department of Labor, 1975).

Based on data from 103 employees, air lead levels of 200 micrograms/m^3 produced a mean blood level of 70 micrograms/100 ml; some workers had over 80 micrograms lead/100 ml in blood (Williams, 1975). Interestingly, the data on air lead and corresponding blood lead levels reported by Short Associates (1976) tends to confirm the relationship described above.

Data correlating somewhat lower blood lead levels, such as 60 micrograms/100 g, to air lead levels are not definitive. Thus, the regression equation relied upon in Williams' study is based upon data which do not contain a critically important value--the blood lead level corresponding to an air lead level of 52 micrograms/m^3.

If it is assumed that the Williams regression equation is correct, an air lead level of 50 micrograms/m^3 would correspond to a mean blood lead level of 40 micrograms/100 g, with an upper limit of approximately 60 micrograms/100 g. However, as noted above, critical data are missing which leaves doubt as to the correctness of this projection. The regression equation is unduly weighted by data at either extreme, and extrapolation of this equation to predict the air lead--blood--lead relationship beyond the limits of measured data is somewhat speculative. In any event, the study by Williams, even with its limitations, provides the best available data with respect to the air lead--blood lead relationship in industrial exposure situations. Clearly, the Williams study shows that to achieve a mean blood lead level of 40 micrograms/100 g would require an 8 hour air lead concentration of less than 150 micrograms/m^3 based on a time-weighted average (U.S. Department of Labor, 1975).

Based on Williams, et al., (1969) calculations, it appears that an increase of 1 microgram/m^3 in the weekly time weighted average concentration of lead in air would correspond to an increase of approximately 1 microgram/100 ml in blood lead.

Prpic-Majic, et al., 1973, and Fugas, et al., 1973, report data for a study of 52 workers in unspecified lead trades. The time weighted average concentration of respirable lead particles was 35 micrograms/m^3; the mean blood lead level of the group was 44.3 micrograms/100 ml. A control group living in an area having air lead at 0.2 micrograms/m^3 and a mean blood lead level of 22.4 micrograms/100 ml was used to establish baseline levels of blood lead due to non-air sources of 22.1 micrograms/100 ml (0.3 micrograms/100 ml in the control group was due to air). Since the air lead level in the occupational environment was 35 micrograms/m^3, it was concluded that 1 microgram of lead per m^3 in air contributes 0.6 micrograms/100 ml of blood (22.1 micrograms/m^3 ÷ 35 micrograms/m^3).

The studies of Prpic and Majic, et al., (1973), Fugas, et al., (1973) and Williams (1975) suggest that the incremental increase in blood lead per unit increase in lead in air is somewhat less at air lead levels characteristic of industry than those in the usual outdoor ambient range (i.e., 0.2-10.0 micrograms/m^3) where an increase of 1 microgram/m^3 in air is said to lead to an increase of 1 microgram/100 ml or slightly greater in blood (U.S. Environmental Protection Agency, 1972; Environmental Health Resource Center, 1973). This finding was also confirmed by Hammond (1977) as discussed in Section 6.5.1 and Table 6.27.

6.5.3.3 Effects of Chronic Exposures on Mortality--

Dingwall-Fordyce and Lane (1963) carried out a retrospective mortality study in a cohort of British workers who retired from work between 1926 and 1960. All members of the study group had at least 25 years of service; workers were classified according to three grades of exposure: "heavy", "medium" or "none" based on average urinary lead concentration records. The heavy exposure group (average urinary lead 100-250 micrograms/liter over the past 20 years of employment) had higher than normal death rates from cerebrovascular diseases. Included in this category are cerebral hemorrhage, thrombosis and arteriosclerosis. Interestingly, the trend of excess deaths in the heavy exposure group was most pronounced among men who retired prior to 1951. Such a finding is most likely related to technological changes which improved exposure conditions. Deaths from malignant neoplasms were not above the rate expected (based on the general population rates) in any of the exposure categories.

Malcolm (1971) also published the results of a mortality study which examined men exposed to lead at "moderate" levels. The average blood lead level of the group was 65 micrograms/100 ml. He found no evidence of significant excess mortality from heart disease, pulmonary disease, cerebrovascular accidents, cancer, renal disease and other miscellaneous causes among the group.

Cooper and Gaffey (1975) undertook a study of men who worked in lead production facilities and battery plants to determine whether or not their mortality patterns differed significantly from those of men not occupationally exposed to lead. This investigation took the form of a retrospective study in six lead-production facilities and ten battery plants. The former included one primary smelter, two refineries, and three recycling plants. A group of 7032 men who had been employed in these plants between 1946 and 1970 was followed to determine whether they were still alive at the end of 1970. Their observed mortality by cause was compared with that of all United States males.

Lead absorption in many of the men was greatly in excess of currently accepted standards based upon urinary and blood-lead concentrations available for a portion of the group. Seventy-eight percent of 47 smelter workers had blood lead levels $\geq$ 80 micrograms/100 ml or more over the period from 1946-1961. After 1965, data based on 489 workers showed 35 percent had blood lead $\geq$ 80 micrograms/100 ml. Levels from the battery workers were somewhat lower than those of the smelter workers. Over all levels of exposure, duration and job classifications, 81.5-95.7 percent of the workers had blood lead levels $\geq$ 40 micrograms/100 ml.

There were 1356 deaths reported; death certificates were obtained for 1267. The standardized mortality ratio (SMR) for all causes was 107 for smelter workers and 99 for battery plant workers indicating a fairly close approximation of the U.S. male population whose SMR = 100 by definition. Deaths from neoplasms were in slight excess in smelters, but not significantly increased in battery plants. There were no excess deaths from kidney tumors. The SMR for cardiovascular-renal disease was 96 for smelter workers and 101 for battery plant workers, i.e., roughly the same as for the general population but not as good as might be expected in an employed population (which commonly has an all-causes SMR of 60-90 percent of that of the general population). There was definitely no excess in deaths from either stroke or hypertensive heart disease. However, deaths classified as "other hypertensive disease" and "unspecified nephritis or renal sclerosis" were higher than expected. The actual numbers of deaths in these last-named categories combined (41 where 19.5 expected) represented about 3 percent of all certified deaths. In these observations, the possible interactive effects between lead and other renal toxic agents such as cadmium cannot be ruled out, however. The life expectancy of lead workers was calculated to be approximately the same as that of all U.S. males.

6.6 ORGANIC LEAD

In general, the alkyl derivatives of lead are highly toxic compounds, and are readily absorbed through the skin. TEL and TML are clear, colorless liquids, volatile, nonpolar, nonionic, and soluble in many organic solvents such as hydrocarbons, chloroform, ether, and absolute ethanol. They have very low water solubilities, and are relatively unreactive in air, water or alkali (Shapiro and Frey, 1968). The high solubility of alkyl lead compounds in body fluids is the basis for toxicity through percutaneous absorption whereas the volatility of these compounds (particularly when added to gasoline) underlies the hazard potential among workers engaged in the production of these compounds. Those chronically exposed to evaporating gasoline may also be at risk, although few studies have been conducted. Because alkyl lead compounds are light-sensitive and undergo photochemical decomposition when they reach the atmosphere; their presence in the atmosphere is transient (National Academy of Sciences, 1972). The full complement of organic lead compounds was identified in Section 2.2.2. Suffice it to say that the most significant organolead compounds from a toxicological viewpoint are the lead alkyls, tetraethyl and tetramethyl. Additionally, a number of lead compounds of organic acids, such as lead naphthenate,lead octoate, etc., used in the paints and plastics industry are significant although these are, by industry convention, classified as inorganic compounds. Their behavior in biological systems also appears more similar to inorganic lead than to that of the lead alkyls.

Lead soaps of organic acids are commonly used as driers by the paint, varnish, printing ink and linoleum industries. Soaps of mixed acids of linseed oil and rosin acids are known as linoleate driers and resinate driers, respectively. Lead stearates, tallates, naphthenates, and octoates (chiefly 2-ethylhexoate) are also produced and marketed in the United States as paint driers. The hazards encountered in the handling and use of driers and metallic soaps are associated with the toxicity of the metal present, the solvents contained, and their activity as oxidation catalysts. Although little data are available regarding the specific toxicities of these compounds, in general, the LD_{50} values appear to be several orders of magnitude higher than those of TEL and TML. While many of the symptoms of acute poisoning by inorganic and organic lead are similar, they can be distinguished diagnostically. Organolead poisoning results in elevated levels of lead in the urine but less consistently in the blood. Likewise, red blood cell stippling, anemia, and alterations in urinary porphyrins are not consistently seen with organic lead exposure, particularly in acute episodes.

In general, the alkyl (tri- and tetraalkyl) derivatives of lead are highly toxic compounds which are absorbed by inhalation, ingestion or percutaneous absorption. These compounds are probably distributed in a nonionic form and, being lipid-soluble, are concentrated in the brain, body fat and liver. Because of this selective distribution, manifestations of lead poisoning are dominated by involvement of the central nervous system and differ from those of inorganic lead poisoning (Gerarde, 1964; Schepers, 1964).

6.6.1 Uptake and Absorption

Kehoe (1925, 1927) showed that tetraethyllead vapor is readily absorbed through the pulmonary epithelium. Using radium-D (^{210}Pb) as a marker, Mortensen (1942) studied the uptake of tetraethyllead in the lungs of rats. The amount absorbed was proportional to the concentration of vapor in the inhaled air, although the proportion decreased at high concentrations (see Table 6.36). Because lead alkyls are broken down by light and heat, their presence in the air is transient and it is believed that they contribute little to the inhalation burden.

Ingestion is a much less probable route for uptake and absorption of organic lead compounds than inhalation and skin absorption. In general, lead soaps are hydrolyzed and possibly converted to metal chlorides and free acids when ingested. Any toxicity would be associated with the metal present (Kirk-Othmer, 1965). The lead content varies somewhat according to the type of metallic soap and also according to the viscosity of the product, ranging from about 18 percent lead in the resinate paste products to approximately 37 percent lead in solid naphthenates. Lead content of the tallates, linoleates, and 2-ethylhexoates are intermediate, averaging from 16-26 percent lead (Payne, 1954). Hazards from inhalation and skin contact may also arise when solvents are combined with the lead soaps, particularly in the liquid driers. In such situations, the solvents probably represent a greater toxicological hazard than the lead in the paint driers. One estimate places the total number of persons directly exposed to lead in the manufacture of paint driers in the United States at less than 250; thus, it is a relatively insignificant source of lead exposure compared to the primary and secondary lead and storage battery industries which employ about 25,000 persons who are potentially exposed to much higher levels (Short Associates, 1976). Further, the usage of many types of paint driers, especially the linoleates, resinates, stearates, and tallates has markedly declined in the past decade, further reducing any possible hazard.

Pettinati, et al., (1959) and Rassetti, et al., (1961) point out that percutaneous absorption is of importance only in the case of lead alkyls and lead salts of naphthenic and fatty acids. Eldridge (1924) reported that tetraethyllead was absorbed rapidly through the skin in both dogs and guinea pigs.

In a study of the rate of percutaneous absorption of tetraethyllead and inorganic lead compounds, Lang and Kunze (1948) found the amount of lead in the kidney from application of tetraethyllead was significantly elevated relative to the controls who received various forms of inorganic lead (Table 6.37).

Tetraalkyl lead compounds are volatile, highly lipid-soluble, and would be expected to pass through biological membranes including the placenta. McClain and Becker (1972) reported that trimethyllead crossed the placental barrier to only a limited extent at low maternal doses. At higher doses, transport was much greater, probably because binding sites in maternal erythrocytes were saturated at the higher dose.

Table 6.36 EFFECT OF CONCENTRATION ON ABSORPTION OF TETRAETHYLLEAD IN RATS[a]

Vapor Concentration, mg/liter	Mean TEL Absorbed, mg/kg	Ratio of Amount Absorbed to Concentration
0.07	0.24	3.4
0.15	0.53	3.5
0.51	1.52	3.0
1.03	3.19	3.1
2.50	6.34	2.5
7.00	16.90	2.4

[a] Source: Mortensen. Reprinted, with permission, from Journal Industrial Hygiene and Toxicology. (c) Williams and Wilkins Co. (1942).

Table 6.37 CUTANEOUS ABSORPTION OF LEAD COMPOUNDS[a]

Compound	Quantity Applied, mg/g	Lead Concentration in Kidneys, Wet Wt.	Control
Arsenate	102	0.85	0.55
Oleate	148	1.30	0.59
Acetate	77	1.80	0.82
Tetraethyl	106	64.20	0.82

[a] Source: Lang and Kunze. Reprinted, with permission, from Journal Industrial Hygiene and Toxicology. (c) Williams and Wilkins Co.

6.6.2 Tissue Distribution

The distribution of the organic lead salts differs markedly from the inorganic salts of lead. Bolanowska (1968) investigated the distribution and excretion of triethyllead in rats following intravenous administration of tetraethyllead. Twenty-four hours after administration of tetraethyllead, 50 percent of the total lead in the internal organs was in the form of triethyllead; the highest levels were found in the liver, blood, kidney, and brain. Cremer (1959) found that tetraethyllead was rapidly converted to triethyllead in the liver. Triethyllead then remained stable *in vivo* for several days before it was excreted in the feces and urine at a rate equivalent to not more than 1 percent of the daily dose. Inorganic lead constituded the remainder of the *in vivo* lead beginning 24 hours after injection.

The triethyllead ion is identified as responsible for the toxic effects of tetraethyllead. There is evidence that tetramethyl- and tetrapropyllead compounds are metabolized to the trialkyl form much more slowly than tetraethyllead is converted to triethyllead. This may account for their being comparatively less toxic, although once formed, trimethyllead compounds are as toxic as the triethyllead compounds (Cremer and Callaway, 1961). Unlike those of inorganic lead, the organic lead compounds have no special affinity for bone but a high affinity for lipoid tissues, especially those constituting the nervous system. Therefore, the central nervous system is the site of greatest concentration.

Schepers (1964) observed that the concentration in the brain is much lower than in the liver and lungs, even though the affects of organic lead compounds are mainly in the central nervous system in experimental animals. After inhalation of toxic amounts of tetraethyllead the concentration of lead in the skeleton and in blood is negligible, whereas after inhalation of toxic amounts of tetramethyllead, the concentration of lead in blood may exceed that in any other tissue including the skeleton. Following inhalation by rats, tetraethyllead can be recovered unchanged from the liver (Stevens, et al., 1956), although it is rapidly metabolized in the liver to inorganic lead so that chronic exposure may result in distribution and in a toxic syndrome characteristic of inorganic lead (Cremer, 1959).

6.6.3 Elimination

There are few data on the excretion of alkyl lead compounds such as tetraethyllead and tetramethyllead. Sanders (1964) states that in both inorganic and organic lead intoxication the urine will probably be found to have an abnormally high concentration of lead. In tetraethyllead intoxication, it is likely to be considerably higher than it is in inorganic lead poisoning since lead absorbed in this manner is more rapidly excreted.

In considering the kinetics of organic lead excretion, it should be noted that TEL and TML have a far shorter residence time in the blood and other tissues than does inorganic lead. Kehoe and Thamann (1931) found that in rabbits, following skin absorption, the absorbed tetraethyllead decomposed in the tissues after a period of 3 to 14 days. Both its distribution and excretion followed quantitatively that of water-soluble lead compounds. In a study of the excretion of triethyllead in rats, Bolanowska (1968) found that 24 hours after the administration of TEL, 50 percent of the total lead in the soft organs was in the form of triethyllead. Triethyllead concentration *in vivo* then remained steady for several days, and was excreted in the feces and urine at a rate equivalent to not more than 1 percent of the daily dose of TEL. Inorganic lead constituted the remainder of the *in vivo* lead 24 hours after TEL injection, and no diethyllead was found, even shortly after administration of TEL. Diethyllead was fairly stable *in vivo*, but less so than triethyllead. Bolanowska notes the presence of triethyllead in humans who died up to 20 days after acute poisoning with TEL.

6.6.4 Toxic Effects

6.6.4.1 Acute Toxicity of Various Organolead Compounds--

The absorption of lipid-soluble alkyl lead compounds, either through the skin or the lungs may result in central nervous system manifestations including insomnia, asthenia, tremors, headache, neuromuscular pain, hallucinations, mania, delusions, and convulsions. The results of the administration of single, lethal doses of TEL or TML progress from hyper-irritability and tremors to convulsions and death. Chronic exposure to alkyl lead also leads to neurotoxicity with similar symptomatology as that following acute exposure.

The toxicities of TEL and TML are shown in Table 6.38, in comparison with those for several inorganic lead compounds. The comparative mortality of rats and dogs following inhalation of TML or TEL is shown in Tables 6.39 and 6.40.

The trialkyl ionic metabolites of TEL and TML are thought to be the toxic lead species. The *in vivo* conversion of tetralkyllead to trialkyllead is well established and is known to occur in the liver of humans. TEL is converted rapidly to the more toxic trialkyl derivative, while the conversion of TML to its trialkyl derivative is much slower. Therefore, the toxicity of the tetraalkyl compounds apparently depends on the rate of conversion to the more toxic trialkyl derivative (Gerarde, 1964).

The intraperitoneal injection of trimethyllead induces in rats signs of central nervous system toxicity (tremors and convulsions) at low doses. The LD_{50} by this route is 25.5 milligrams per kilogram. The intraperitoneal LD_{50} for triethyllead in rats is 11.2 milligrams per kilogram, and the intravenous LD_{50} in rats for tetraethyllead is 15.4 milligrams per kilogram (Gerarde, 1964). Tetramethyllead is less toxic than trimethyllead, and a dose of 34 milligrams per kilogram given intravenously to rats causes no signs of poisoning. Large, oral doses of tetramethyllead (250 to 500 milligrams per kilogram) fed to rats produced signs of intoxication identical to those elicited by trimethyllead. An immediate toxic reaction was observed in rabbits dosed intraperitoneally with 7.5 and 15 milligrams per kilogram of trimethyllead. The intravenous dosing of 20 and 40 milligrams of tetramethyllead did not produce toxic manifestations in the rabbit (Gerarde, 1964).

Table 6.38 TOXICITIES OF SOME LEAD COMPOUNDS[a]

Compound	Animal	Route	Toxic Dose	Dosage Compound, mg/kg	Dosage Metal, mg/kg
Lead metal (powder)	Rat	IP	LD	-	1000
Lead acetate	Rat	IP	LD_{50}	150	95
	Rabbit	IV	LD	50	32
	Dog	IV	LD	300	191
Lead carbonate	Guinea pig	Oral	MLD	1000	860
Lead dioxide	Guinea pig	IP	LD_{50}	220	173
Lead nitrate	Rat	IP	LD	270	169
Tetraethyllead	Rat	IP	MLD	10	6.4
	Rabbit	SC	MLD	32	20.4
	Rabbit	IV	MLD	22	14
Tetramethyllead	Rat	Oral	LD_{50}	108	83

[a] Adapted from Venugopal and Luckey (1975) and Schepers (1964).

Table 6.39 COMPARATIVE MORTALITY OF RATS FOLLOWING INHALATION OF TETRAMETHYLLEAD OR TETRAETHYLLEAD, AND LEAD CONTENT OF THEIR TISSUES[a]

Compound	Concentration of Compound in Air Breathed, mg/m^3	Duration of Exposure hours	Mortality (Died/Exposed)			Average Interval between Last Period of Exposure and Death, days	No. Pooled for Chemical Analysis	Average Concentration of Pb in Major Viscera,[b] mg/100 g	Average Concentration of Pb in Urine, mg/liter
			M	F	Total				
Tetramethyllead	63.0	10 X 7	5/5	4/5	9/10	2	5	10.12	-
	49.0	18 X 7	5/5	4/5	9/10	0.25	8	10.06	8.38
	22.0	35 X 7	5/5	3/5	8/10	2	8	7.54	4.53
						1[c]	4	5.47	
	12.0	150 X 7	4/5	0/5	4/10	0.50[c]	3	2.25	1.94
						40[c]	3	0.67	
Tetraethyllead	46.0	5 X 7	3/5	5/5	8/10	3	8	1.99	-
	22.0	14 X 7	4/5	5/5	9/10	0.25	9	2.99	-
	12.0	150 X 7	0/5	0/5	0/10	1[d]	4	0.78	5.22
						39[d]	5	0.43	
Control	0	150 X 7	0/10	0/10	0/20	12	20	0/12	0.39

[a] Source: Gerarde. Reprinted with permission from Annual Reviews Pharmacology. (c) Annual Reviews, Inc., 1964

[b] Viscera included: lung, liver, kidney, spleen, heart, and brain.

[c] Of the ten rats that inhaled 12 mg per cubic meter, four died after 116 periods. These fatalities were complicated by intercurrent infections. Three of the remainder were killed one-half day after the 150th period, and the remaining three were killed 40 days later.

[d] Killed for further examination.

Table 6.40 COMPARATIVE MORTALITY OF DOGS FOLLOWING INHALATION OF TETRAETHYLLEAD, AND LEAD CONTENT OF THEIR TISSUES[a]

Compound	Inititial Body Weight, kg	Concentration of Compound in Air Breathed, mg/m^3	Duration Exposure Before Fatal Outcome, hours	Average Interval Between Last Period of of Exposure and Death, days	Average Concentration of Pb in Major Viscera,[b] mg/100 g	Average Concentration of Pb in Urine, mg/liter	Average Concentration of Pb in Blood, mg/100 g
Tetramethyllead	10.8	44.0	8 X 7[c]	1	1.03	4.02	00.13
	9.0	23.0	9 X 7	0	0.85	4.52	0.05
	5.4	12.0	15 X 7	1	0.69		
	11.0	12.0	14 X 7	2	0.74	0.64	0.04
	11.6	4.0	107 X 7	0	0.79		
	11.0	4.0	84 X 7	0	-	0.59	0.06
Tetraethyllead	10.6	42.0	7 X 7[c]	0.25	1.22	10.20	0.12
	13.2	22.0	30 X 7	0	2.96	2.29	0.14
	5.9	12.0	29 X 7	3	1.02		
	10.2	12.0	24 X 7	0	0.67	2.42	0.06
Control	6.8	0	>130 X 7	-	0.05	0.16	0.02

[a] Source: Gerarde. Reprinted with permission from Annual Reviews Pharmacology. (c) Annual Reviews, Inc., 1964.

[b] Viscera included: lung, liver, kidney, spleen, heart, and brain.

[c] Each line represents the period of survival of a single dog subjected to exposure to an alkyllead compound. (Two control dogs were killed at the end of the period of time indicated).

6.6.4.2 Neuropathology--

The pathological lesions noted in lead induced CNS anomalies include cerebral edema, encephalopathy, increased cerebrospinal fluid pressure, proliferation and swelling of endothelial cells, dilation of capillaries and arterioles, glial cell proliferation, focal necrosis and neuronal degeneration. (Goyer and Rhyne, 1973).

Many of these symptoms are also common to inorganic lead poisoning as well.

One investigator has attempted to distinguish between CNS toxicity caused by organic and inorganic lead compounds. This is the monograph prepared by Pentschew (1958) based principally on earlier work of Tolgskaya and Reznikov (1955). These authors discussed the physiologic differences between encephalopathy caused by organic lead compounds versus that attributable to inorganic lead. It is notable that TEL encephalopathy is characterized by insufficient vascular tension. The fact that inorganic lead attached to the ethyl radical is incapable of exerting its pressure-increasing action on vessels is probably connected with the simultaneous onset of disturbances of the central blood pressure regulation in the direction of hypotension. For this reason the epileptic attacks, so characteristic as a sign of inorganic lead encephalopathy, are absent in TEL poisoning. Some relationship probably exists also between blood pressure and vascular tension and the increase in brain volume in the form of edema and swelling of the brain. This is generally absent in TEL encephalopathy.

Other indications that the lesions themselves may not be similar in organic and inorganic poisoning are the reports that following recovery from TEL encephalopathy, a large part of the damage is reversible since many experience complete remission of neurologic and psychic symptoms associated with TEL poisoning. This is not the case with inorganic lead encephalopathy, especially in children, where permanent neurological sequellae are to be expected.

Niklowitz (1974) investigated the ultrastructural effects on nerve cell components of selected brain areas (frontal cortex, cerebellum, hippocampus) after exposure of rabbits to tetraethyllead (TEL).

A single dose of 100 milligrams per kilogram of TEL led, after a latency period of 12 to 18 hours, to neurological disorders such as convulsions, and produced significant lesions of components of pyramidal cells and atroglial cells. These developed before the onset of major neurological signs of toxicity.

Two types of degenerative cell changes were identified: cellular pyknosis and cellular hydrops, each specific to certain cell layers of selected brain areas. The subcellular manifestations of nerve cells undergoing hydropic degeneration exhibit a distinct pattern. The following sequence of appearance of structural alterations was determined: (1) folding of the nuclear membrane; (2) swelling and severe lesions of mitochondria; (3) hypertrophy of Golgi complexes; and (4) patchy chromatolysis of the ergastoplasm. Progressive hypertrophy of Golgi saccules and vacuolization of ergastoplasm areas lead to a vacuolar hydropic degeneration of affected nerve cells.

In each brain area an accumulation of lead of approximately 150 nanomoles per gram dry weight took place after exposure of rabbits to TEL. Simultaneously, a statistically significant decrease occurred in the content of copper, iron, and zinc.

Cytomorphological measures were not made at the same time intervals as measures on trace metals. Niklowitz and Yeager's metal analysis (1973) in these rabbits showed that they received TEL 100 mg/kg intraperitoneally and were decapitated after showing clinical signs of convulsions. The histopathology study was a time course event preceding convulsions and the metal analysis study was at height of toxic response. It would not be surprising that many other measures of brain chemistry at the time of convulsion following a lethal dose of TEL show changes relative to non-treated animals.

Rats injected with leaded gasoline (1,000 ppm of tetraethyllead per 100 grams of body weight) showed excessive tension and excitement by the 6th or 7th day. One to 3 days after both leaded gas and nonleaded white gas injections, the delta, theta, and alpha brain waves decreased significantly. The electrocorticogram from 6 to 7 days after leaded gasoline injection showed marked alpha and theta waves suggestive of the direct action of triethyllead on the brain stem reticular formation (Saito, 1973). 1 mg TEL per 100 g body weight (10 mg/kg i.p.) is the minimum lethal dose (MLD) for the rat. While it is reasonable to study the toxicity of high doses of intoxicants (TEL) in attempts to understand mechanism of action, the neuronal effects or electrical activity elicited at near lethal doses may be totally absent at reasonable environmental doses. The author's suggestion that TEL has a direct effect on brain stem reticular system without discussing dose effect relationships has limited meaning.

Triethyllead inhibits catecholamine effect on smooth muscle contraction. Consequently, there has been some speculation that the toxicity of triethyllead and particularly its action on the central nervous system can be explained by a combination of effects which might result from an upset of cholinergic and adrenergic central pathways due to the formation of endogenous psychotogenic complexes. This speculation is based on unconfirmed claims that adrenochrome, which is an intermediate in the conversion of catecholamines to trihydroxyindole products, is an hallucinogenic agent. Galzigna, et al., (1973) found that triethyllead dramatically increases the duration of the succinylcholine-induced myoneural block of cholinergic transmission. This is explained by the competition between triethyllead and succinylcholine for serum cholinesterase. Triethyllead is able to antagonize the effect of norepinephrine in vivo but alone is without any effect on normal contractile activity.

6.6.4.3 Metabolic Effects--

Few studies have focused specifically on the metabolic effects of alkyllead compounds.

Trimethyl- and triethyllead decrease oxygen consumption when added to rat brain and cortex slices *in vitro*. Tetramethyl- and tetraethyllead did not have this effect except at much higher concentrations (amount unknown). A decrease in *in vitro* oxygen consumption was also found in brain slices taken from rats previously exposed to triethyl- and tetraethyllead (Gerarde, 1964). Glucose metabolism in brain slices is also inhibited by the diethyl-, triethyl-, tripropyl- and trimethyllead compounds.

TEL has effects on neurotransmitter metabolism in the brain of experimental animals (Cremer and Callaway, 1961). The mechanism of this action was studied by assessing the effects of triethyllead *in vitro* on the cholinesterase activity of rat diaphragm and *in vivo* on serum cholinesterase in the dog. The highest inhibition of acetylcholinesterase activity of the rat diaphragm obtained with two concentrations (0.4 and 0.8 milliliter) of the substrate acetylthiocholine was about 25 percent of normal activity. The inhibition was noncompetitive. As with other aspecific cholinesterase inhibitors, triethyllead was able to induce a maximal inhibition of 25 to 30 percent on the true cholinesterase activity of the rat diaphragm preparation. Maximum inhibition of serum cholinesterase was observed 15 minutes after the administration of 6 milligrams per kilogram triethyllead to dogs and full recovery occurred 45 minutes after administration (Galzigna, et al., 1973).

6.6.4.4 Enzyme Effects--

In view of the high sensitivity of ALAD to lead, the levels of enzyme activity in the blood of men occupationally exposed to lead alkyls, particularly tetraethyllead, were measured (Miller, et al., 1972). The enzyme activity in an exposed group of men was significantly less (P less than 0.001) than in a control group, the respective mean values being 220 and 677 units of enzyme activity.

Tetraethyllead is metabolized in the body via triethyllead and diethyllead ions. Diethyllead ion was found to inhibit ALA dehydratase activity at concentrations greater than 5×10^{-5} M, although the degree of inhibition was less than that obtained with Pb^{++}. These results suggest that exposure to tetraethyllead can cause a decrease in erythrocyte ALA dehydratase activity (Miller, et al., 1972). The effect of known inhibitors on ALA dehydratase activity, such as alcohol consumption and cigarette smoking were not taken into account in the group of workers investigated.

6.6.5 Epidemiologic Studies

Gerarde (1964) states that because of the large dilution factor (3 to 4 milliliters per gallon of gasoline) of TEL, the normal use of "leaded" gasoline does not present a lead intoxication hazard. However, human exposure to TEL during the cleaning of leaded-gasoline tanks has led to fatalities (Shapiro and Frey, 1968). Robinson (1974) has presented evidence of absorption of alkyl lead antiknock compounds among occupationally exposed workers. Delta-aminolevulinic acid and lead were measured in the urine of 123 men of various ages and lengths of service, all working as operators or maintenance men in an area of production of alkyl lead antiknock compounds (tetraethyllead and tetramethyllead). Results are shown in Figure 6.21. The levels of ALA and lead in urine were found to have a relatively low positive correlation of 0.52. Figure 6.22 suggests that a given elevation of urinary lead excretion probably is associated with a lower level of urinary ALA excretion when the exposure is to organic lead.

It is not clear whether this difference might be related primarily to differences in circumstances of exposure or to differences in metabolism (biotransformation) due to exposure to a different form of lead. For example, there have been no experimental studies reported to indicate what effect, if any, tetraethyllead or tetramethyllead might have on porphyrin metabolism and, hence, on urinary ALA excretion. In summary, the investigation by Robinson (1974) shows that absorption of organic lead as indicated by increased urinary levels, is associated with an increase in urinary ALA levels. However, the mechanism through which this effect is produced was not identified.

Proper protection of workers has virtually eliminated the problem of TEL or TML poisoning over the last 30 years. Robinson (1976) made a detailed comparison of extensive medical information (results of periodic medical examinations, of medical records of absence from work due to nonoccupational illness, and of cumulative medical diagnoses) for workers with 20 years or more tetraethyllead (TEL) service to a matched (for age, sex, race, and length of service) group of workers with no occupational lead (TEL or other) exposure. The comparison showed no significant health differences between the two populations. Table 6.41 shows the results of the cumulative diagnoses. The conclusion was that, under the conditions that have existed at the Baton Rouge, Louisiana, plant, workers having long occupational exposure to levels of lead (chiefly TEL) sharply in excess of that of the general public, but within a range termed "safe" by current industrial medical standards, have not suffered detectable impairment of health.

In cities alkyl lead levels were reported "not to reach 10 percent of inorganic levels" (National Academy of Science, 1972). In fact, much of the lead burned in gasoline (see Section 7.4.1) is not exhausted in forms which can remain suspended in the atmosphere. To date, no information exists on the effects of chronic, low-level exposure to airborne alkyl lead.

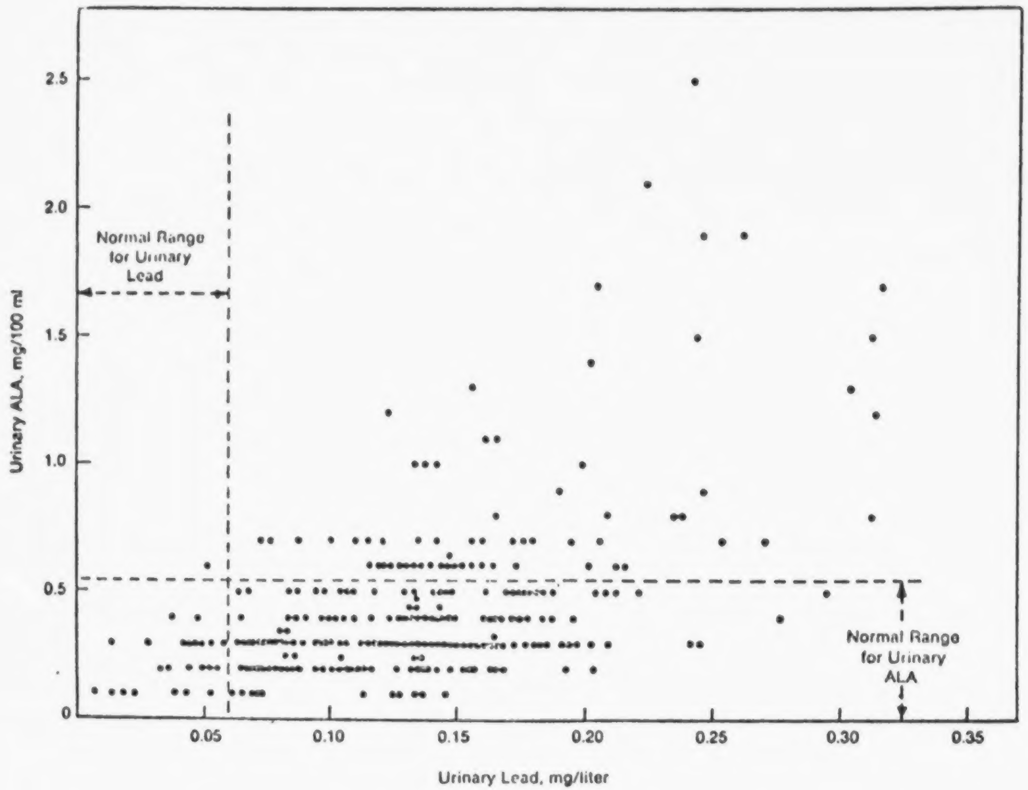

Figure 6. 21 Lead and ALA levels in urine of organic lead (TEL, TML) workers. Source: Robinson. Reprinted with permission from Archives of Environmental Health. (c) American Medical Association, 1974.

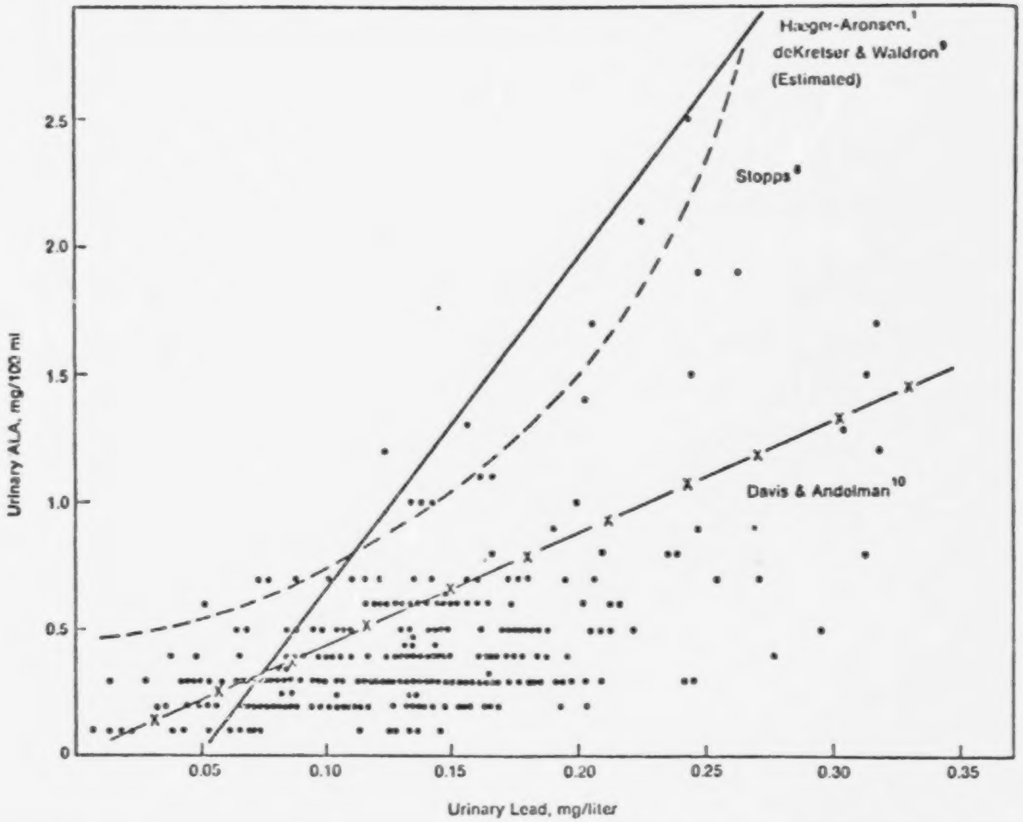

Figure 6. 22 Comparison of reported urinary ALA-lead relationships for exposures to inorganic lead with results of present study involving organic lead (TEL, TML). Source: Robinson. Reprinted with permission from Archives of Environmental Health. (C) American Medical Association, 1974.

Table 6.41 CUMULATIVE DIAGNOSES OF TEL WORKERS VS NON-TEL WORKERS,[a,b]

Diagnosis	TEL		NonTEL	
	No. Men	Percent	No. Men	Percent
Hypertension	18	12.9	27	19.4
Myocardial infarction	3	2.2	5	3.6
Angina pectoris (without MI)	2	1.4	3	2.2
Arrhythmia (only)	2	1.4	1	0.7
Abnormal EKG (only)	1	0.7	7	5.0
Cerebrovascular disease	1	0.7	-	-
Other peripheral artery disease	1	0.7	2	1.4
Phlebitis, thrombophlebitis	5	3.6	4	2.9
Anemia	1	0.7	-	-
Polycythemia	-	-	1	0.7
Other blood disease	-	-	-	-
Pyelonephritis	3	2.2	2	1.4
Other renal disease (except stones)	-	-	3	2.2
Renal stones	7	5.0	12	8.6
Liver disease	2	1.4	4	2.9
Gallbladder disease	4	2.9	3	2.2
Gastric or duodenal ulcer	16	11.5	18	12.9
Colitis	-	-	-	-
Chronic lung disease	5	3.6	2	1.4
Peripheral neuritis	1	0.7	-	-
Alcoholism	2	1.4	-	-
Neuropsychiatric	1	0.7	3	2.2
Thyroid disease	-	-	2	1.4
Diabetes mellitus	3	2.2	7	5.0
Gout	4	2.9	3	2.2
Rheumatoid arthritis	-	-	1	0.7
Lumbago	22	15.8	26	18.7
Cancer of skin	7	5.0	4	2.9
Other cancer	-	-	-	-
Glaucoma	1	0.7	3	2.2
Cataracts	-	-	-	-
Obesitv, 20-29 percent	42	30.2	29	20.9
Obesity $\geq$ 30 percent	40	28.8	39	28.1
No diagnosis	22	15.8	29	20.9
Obesity only diagnosis	37	26.6	22	15.8
Total Diagnoses	194	-	211	-
Diagnoses per person	-	1.4	-	1.5

[a] Source: Robinson. Reprinted with permission. (c) Journal of Occupational Medicine, 1976.

[b] 139 persons each group, 20 (or more) years.

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7.0 ENVIRONMENTAL DISTRIBUTION AND TRANSFORMATION

7.1 SUMMARY

Lead occurs only to the extent of about 16 ppm of the earth's crust; however, its ores (which are the source of primary lead) are concentrated in reasonably large deposits. U.S. production of lead from domestic ores in 1975 was 560,000 metric tons (621,000 short tons). World production during 1973 was 6.9 million metric tons (7.6 million short tons). U.S. consumption of primary and secondary lead during 1975 was 1.17 million metric tons (1.3 million short tons). Nearly one-half of the total used (597,000 metric tons) was secondary lead. Secondary lead is obtained from storage batteries and alloys.

The major uses of lead are in the manufacture of antiknock additives for automotive fuels, storage batteries and accessories, pigments, ammunition, and solder. Minor uses include cable coverings and pipes, alloys with antimony, copper and tin, sheet lead, and bearing metals.

Extremely high soil and dust fall levels of lead have been found around secondary smelters. However, the monthly geometric means of the air lead concentrations close to the smelters averaged 1 to 5.3 micrograms per cubic meter of air, and were only about double those for urban sites (0.8 to 2.4 micrograms per cubic meter).

It is estimated that before the industrial revolution, the lead content of marine waters was about 0.02 to 0.04 parts per billion (ppb). At the present time oceanic surface waters contain about ten times that much lead. The lead content of inland lakes and rivers of the U. S. has been found to be of the order of 10 to 50 ppb. Lead-mining areas show the highest concentrations in surface waters with some localities exceeding the 50 ppb limit imposed by the U.S. Public Health Service. Lead-based industries can contribute large amounts of lead to nearby streams depending on the processing of the plant effluents. Up to 800 ppb has been detected in unfiltered water from lead smelter tailings ponds. In drinking water the main source of contamination is the use of lead pipes in older plumbing. Occasionally this may result in levels above the permissible limit, particularly if the water is soft and the pH is below 7.0.

Secondary smelters, automobile exhausts, and houses where lead paint has been used on the exterior, are considered major sources of soil contamination with lead. Lead levels of 16,000 to 40,000 micrograms per gram of soil have been found around a secondary smelter. These values declined to background levels within 300 to 400 meters of the stack. Although the high concentrations of lead in the soil near houses may be due to weathering of lead-based paints, there also is strong evidence that automobile exhausts contribute to soil lead near the roadway. Greatly elevated levels of lead have been found in soils and vegetation along rights-of-way of lead ore truck routes. Contamination generally was limited to a distance of 100 meters or less from the road. The concentrations of lead in street dust from 77 midwestern cities in the U.S. assayed 1,500 to 2,400 milligrams per kilogram (ppm) of dust. Since levels in industrial areas averaged approximately 1,600 milligrams per kilogram of dust, vehicular sources appear to be major contributors.

Large amounts of lead can be found in the soil near roadways as the automobile exhaust provides enough lead to raise the concentration to 400 to 500 ppm. An even greater concentration of lead in soils can be found in the vicinity of houses where lead paint has been used on the exterior. Concentrations of several thousand ppm may exist in the soil immediately adjacent to the house.

The persistence of lead which has been dispersed in the atmosphere depends on the physical form of the lead and on meteorological factors. In general, about half the particulate lead from automotive sources is removed from the air by gravitational effects and is deposited near the roadway. About 30 percent of the lead consumed stays in the oil, oil filter, and muffler. The remaining lead consists of aerosols that remain in the atmosphere until brought down by precipitation. The average residence time of lead in the atmosphere has been found to be about 10 days.

Apparently a significant portion of the lead introduced into surface waters by precipitation and runoff is not soluble and consequently is removed from the water by sedimentation. Probably more important is the absorption of lead in soil particles. Precipitation and contamination by fallout from industrial and vehicular sources also increase the lead content of soils. However, little of this lead enters healthy plant life because it is not present in a readily available form. Contamination of surface soil by inorganic forms of lead may be subject to rapid leaching by water, and under some circumstances lead can be removed fairly rapidly in this fashion. Lead contamination of water by the leaching of landfills could become a problem if the soil chemistry of lead is favorable.

Wastewaters entering treatment plants have been found to contain from about 100 to 1,000 micrograms per liter of lead depending on the industrialization and the automobile traffic density of the area. Waste-waters discharged into coastal waters can bring the lead concentration in harbors up to several hundred micrograms per liter. The effluent from sewage treatment plants usually contains substantially less lead than the incoming wastewater. The primary effluent may contain only half as much lead, and the secondary effluent from one-fifth to one-fourth as much. The lead then is removed with the sludge, where it may constitute a problem if the sludge is spread on agricultural land. However, in actual field operations and in laboratory tests in which some metal toxicity has been observed in terms of reduced growth of plants, lead has not been found to be the cause of the toxicity.

Lead introduced into lakes and streams concentrates in the sediments. It is rapidly removed from water when it passes through soil and bottom sediments. This is due to the high capacity of organic matter to bind the lead more firmly.

The amount of lead in sediments has increased by about a factor of ten in the last 80 to 100 years in populated areas. Concentrations of several hundred ppm by weight of lead have been found in the upper layers of sediments. In areas in which lead has been mined, the lead concentration in sediments can be several thousand ppm by weight.

In a position paper on the health implications of airborne lead, the U.S. Environmental Protection Agency has pointed out that man-made sources of lead contribute most of the lead entering the environment, and that the combustion of leaded gasoline is the single most significant contributor. Accordingly, reduction of airborne lead constitutes an accessible means for reducing potential human exposure to environmental lead.

As can be inferred from data on the projected projection and consumption of lead for lead alkyls, environmental lead from the combustion of gasoline will continue to decline. In 1977, 190,000 metric tons of lead will be used in the production of lead alkyls, 145,000 tons of which will be used domestically, with the remaining 45,000 tons being exported. However, by 1985 projections are for 90,000 tons divided equally between domestic consumption and exports. These estimates assume that, (1) lead additions will not be significantly below the 0.5 g/gal mandated by EPA regulations, and (2) exports of lead alkyls will continue at present levels.

A large number of organometallic compounds of manganese have been investigated as antiknock agents. Of these, probably methylcyclopentadienylmanganese tricarbonyl is the most satisfactory. However, it is not marketed as a primary antiknock but is included in several antiknock blends.

7.2 PRODUCTION AND USES OF LEAD

Lead, one of the oldest known metals, occurs only to the extent of about 16 ppm of the earth's crust (8 and 20 ppm, respectively, in alkaline and acidic rocks) or 15 grams per ton (de Treville, 1964). Its ores which occur chiefly as sulfide in galena (86.8 percent Pb), carbonate in cerussite (77.5 percent Pb), and sulfate in anglesite (68.3 percent Pb) are concentrated in reasonably large deposits. Lead is produced commercially by roasting galena in an oxidizing atmosphere.

Lead is introduced into the environment as a result of the many uses to which it is put by man. Consequently, the amount of lead produced and its distribution among the various applications are important to environmental considerations. Data on the production of lead in the United States for the 7-year period, 1969-75, are presented in Table 7.1 (Ryan and Hague, 1974; 1976).

TABLE 7.1 PRODUCTION AND CONSUMPTION OF LEAD[a]
(Short tons unless otherwise specified)

	1970	1971	1972	1973	1974	1975
United States:						
Production:						
Domestic ores, recoverable lead content	571,767	578,550	618,915	603,024	663,870	621,464
Value------------------thousands-----	$178,609	$159,679	$186,046	$196,465	$298,742	$262,230
Primary lead (refined):						
From domestic ores and base bullion---------------------------	528,086	573,022	577,398[b]	567,256	673,024	530,215
From foreign ores and base bullion	138,644	76,933	103,001	107,260	92,946	105,907
Antimonial lead (primary lead content)------------------------------	11,655	16,116	8,185	13,223	9,867	2,215
Secondary lead (lead content)----------	597,390	596,797	616,597	654,286	698,698	658,456
Exports of lead materials excluding scrap	7,747	5,925	8,376	66,576	61,982	21,256
Imports, general:						
Lead in ore and matte------------------	112,406	65,998	101,514	102,483	94,299	87,560
Lead in base bullion-------------------	296	41	895	4	831	462
Lead in pigs, bars, and old------------	251,480	198,970	245,625	180,788	119,197	105,876
Stocks December 31 (lead content):						
At primary smelters and refineries	192,985	121,660	145,573	89,847	121,051	156,330
At consumer plants---------------------	133,502	125,577	118,544	124,121	166,589	133,315
Consumption of metal, primary and secondary---------------------------------	1,360,552	1,431,514	1,485,254	1,541,209	1,599,427	1,297,098
Price: Common lead, average, cents per pound[c]--------------------------------	15.69	13.89	15.03	16.29	22.53	21.53
World:						
Production:						
Mine---------------------------------	3,741,546[b]	3,742,950	3,802,086	3,852,190	3,832,499	3,787,804
Smelter------------------------------	3,628,422[b]	3,590,730	3,744,660	3,800,753	3,858,205	3,713,691
Price: London, common lead, average, cents per pound---------------------	13.76	11.52	13.68	19.47	26.83	18.73

[a] Adapted from Ryan and Hague (1974;1976).
[b] Revised.
[c] Quotation for 1969-71 at New York and for 1972 and 1973 on a nationwide, delivered basis.

The consumption of lead in the United States by product usage for the years 1972-75 is shown in Table 7.2 (Ryan and Hague, 1974, 1976). Its use in storage batteries utilizes by far the largest amount (634,000 metric tons or 699,000 short tons in 1975), but approximately one-half of this was salvaged from old batteries and the lead recycled. Gasoline antiknock additives, tetraethyllead and tetramethyllead (Section 2.2.1), comprised the second largest use in 1975 (189,200 metric tons or 208,600 short tons). The annual increase in lead consumption in the U.S. during the 10-year period 1962-1971 averaged 2.9 percent, resulting largely from an increased demand for batteries and gasoline additives (U.S. Environmental Protection Agency, 1973).

The trend to unleaded gasoline reduced the lead used for antiknock compounds by approximately 38,000 metric tons (16.7 percent) in 1975 from 1974 consumption, which was itself down about 8.7 percent from 1973. This trend can be expected to accelerate as new cars operating on unleaded gasoline replace older cars on the road. Also, a trend toward smaller and more economical cars contributed to a declining rate of growth of gasoline consumption.

Until recently, uses of lead in pigments and for a variety of metal products applications have accounted for the remainder of the lead that is consumed.

Lead is employed for containers in tank linings for many corrosive liquids. The metal and its alloys are used in solders, type metal, bearings, pipe, cable covering, plumbing, and ammunition. Lead is very effective as a sound absorber, serves as a radiation shield around X-ray equipment and nuclear reactors, and is used to absorb vibration.

There are various uses for specific lead compounds. The major use for lead oxide, PbO, is in the preparation of storage battery plates. The partially oxidized material (black oxide of lead) is preferred. The most extensive use for the fully oxidized PbO is in the manufacture of glasses, glazes, and vitreous enamel.

Another important oxide of lead is red lead or minium, Pb_3O_4. Much of this material is used in the manufacture of storage batteries, but a significant amount forms the pigment for red lead paint which is used in large quantities as a corrosion-resistant coating on iron and steel. Cutting and welding of steel which has been protected in this fashion result in the volatilization and decomposition of the lead oxide and consequently constitute a health hazard in the absence of precautionary measures.

Lead dioxide, PbO_2, is used as the positive plate of the lead storage battery. PbO_2 is used as an oxidizing agent in the manufacture of dyes, chemicals, matches, pyrotechnics, and synthetic rubbers (Klug and Brasted, 1958).

In past years, paint pigments consumed a great deal of the lead output. Several of the most stable inorganic colors were based on lead compounds, and many of the older homes and items of furniture were painted with these

TABLE 7.2 LEAD CONSUMPTION IN THE UNITED STATES, BY PRODUCT[a]
(Short tons)

Product	1972	1973	1974	1975
Metal products:				
Ammunition------------	84,699	81,479	87,090	75,081
Bearing metals--------	15,915	15,657	14,609	12,184
Brass and bronze------	19,805	22,735	22,240	13,404
Cable covering--------	45,930	43,005	43,426	22,099
Calking lead----------	22,483	20,057	19,739	14,296
Casting metals--------	7,139	7,220	7,507	7,711
Collapsible tubes-----	4,020	2,860	2,488	2,216
Foil------------------	4,592	4,985	4,404	3,205
Pipes, traps, bends---	17,780	21,291	16,455	14,233
Sheet lead------------	23,667	23,394	21,294	24,859
Solder----------------	71,289	71,770	66,280	57,344
Storage batteries:				
Battery grids, posts, etc--------	347,225	365,557	391,479	326,714
Battery oxides------	379,367	403,890	460,402	372,700
Terne metal-----------	504	2,658	2,300	1,511
Type metal------------	19,944	21,922	20,516	16,211
Total---------------	1,064,359	1,108,480	1,180,229	963,768
Pigments:				
White lead------------	2,814	1,749	1,996	2,498
Red lead and litharge------------	69,799	89,577	96,163	65,457
Pigment colors--------	16,264	16,963	17,336	10,618
Other[b]----------------	377	477	718	499
Total---------------	89,214	108,766	116,213	79,072
Chemicals:				
Gasoline antiknock additives-----------	278,340	274,410	250,502	208,605
Miscellaneous chemicals----------	849	944	708	181
Total---------------	279,189	275,354	251,210	208,786
Miscellaneous uses:				
Annealing-------------	4,239	3,974	4,097	2,629
Galvanizing-----------	1,397	1,294	1,664	1,228
Lead plating----------	638	744	498	376
Weights and ballast---	21,302	20,848	21,418	20,018
Total---------------	27,666	26,860	27,677	24,251
Other, unclassified uses	24,826	21,749	24,098	21,221
Grand total[c]----------	1,485,254	1,541,209	1,599,427	1,297,098

[a] Adapted from Ryan and Hague (1974;1976).
[b] Includes lead content of leaded zinc oxide and other pigments.
[c] Includes lead which went directly from scrap to fabricated products.

lead colors. Lead chromates have provided yellow, orange, and red pigments. The normal chromate, $PbCrO_4$, is the brilliant pigment chrome yellow. By formulating with alkalis to make basic lead chromates, the oranges can be obtained. The chrome reds can be obtained by making the basic lead chromate from white lead instead of from the usual lead acetate solution. The many gradations of color between yellow and red are obtained by formulating mixtures of the different lead chromates. Chrome green, the most important green pigment, is actually a mixture of yellow lead chromate and Prussian blue.

The oldest white paint pigment, basic lead carbonate, $2PbCO_3 \cdot Pb(OH)_2$, commonly known as white lead, has been used extensively in the past for both interior and exterior white paints for dwellings. However, a series of Federal laws, beginning with the Lead Based Paint Poisoning Prevention Act (LBPPPA), have effectively eliminated lead based paints from this market. The LBPPPA was first enacted in 1971 (P.L. 91-695) to deal with the problems of childhood lead poisoning caused by the ingestion of lead-based paints. The original act prohibited, after January 13, 1971, the use of lead-based paint in residential structures constructed or rehabilitated by the Federal government, or with Federal assistance in any form. The term "lead-based paint" was defined as any paint containing more than 1 percent lead in the dried paint film.

The LBPPPA was amended in 1973 (P.L. 93-151), which among other things redefined "lead-based paint" to mean any paint with over 0.5 percent lead in the dried film. The LBPPPA was again amended in 1976 by enactment of the National Consumer Health Information and Health Promotion Act (P.L. 94-317). Under this Act the Consumer Product Safety Commission issued on August 10, 1976, (41 FR 33636) proposed regulations governing lead-based paint and certain other consumer products, banning as hazardous products:

(1) Lead-containing paint and similar surface-coating materials containing more than a safe level of lead.

(2) Toys and other articles intended for use by children bearing lead-containing paint or other similar surface-coating material containing more than a safe level of lead.

(3) Articles of furniture bearing lead-containing paint or other similar surface-coating materials containing more than a safe level of lead.

On February 16, 1977, (42 FR 9404), The Consumer Product Safety Commission announced its decision that available scientific information is insufficient to establish that a level of lead in paint above 0.06 percent but not over 0.5 percent is safe. The result of this decision is to classify any paint manufactured after June 22, 1977 containing more than 0.06 percent lead as lead-based paint, under the Lead-Based Paint Poisoning Prevention Act (LBPPPA).

Final regulations were issued September 1, 1977, (42 FR 44192) confirming the proposed regulations. Certain exceptions were made for a few specialized coatings not used by consumers and with little likelihood of access to children. These included a number of agricultural and industrial equipment coatings, traffic paints, graphic art coatings, and touch-up coatings for appliances, etc.

Pursuant to these various pieces of legislation to control exposure to lead-based paints in dwellings, the Department of Housing and Urban Development (HUD) issued July 13, 1976, (41 FR 28876) regulations revising 24 CFR Part 35 governing numerous controls on HUD-associated housing constructured prior to 1950. These regulations, among other things:

(1) Require HUD to notify purchasers and tenants of HUD-associated housing constructed prior to 1950 of the hazards of lead-based paint poisoning.

(2) Prohibit the use of lead-based paint in HUD-associated housing.

(3) Provide for the elimination, to the extent practicable, of lead-based paint hazards in HUD-associated housing (and similarly in Federally-owned housing prior to sale for residential habitation).*

In the area of insecticides, lead arsenate was employed as the acid salt, $PbHAsO_4$. In the World War II era hundreds of millions of pounds of this compound were produced for the control of the gypsy moth. The production and usage of lead arsenate have been declining, as the advent of the organic pesticides has resulted in replacement of lead arsenate by other compounds. Total lead consumption in 1975 for all miscellaneous lead chemicals (see Table 7.2) was only 164 metric tons (181 short tons). However, the lead content of soils in orchards and similar agricultural areas is probably the result of the accumulation of lead over the many years of usage of lead arsenate.

Organolead compounds such as hexamethyldilead are used in the manufacture of organolead intermediates. A large number of alkyl- or aryl-substituted lead acetate derivatives such as tributyllead acetate, triethyllead acetate and triphenyllead acetate are used as fungicidal agents in paints (Shapiro and Frey, 1968; Section 4.2.2.2).

Either directly or indirectly, virtually 100 percent of the tetraethyllead (TEL) produced in the United States is used to make antiknock additives for gasolines. The usage pattern for tetramethyllead (TML) is identical with that for TEL except it is preferentially used in aviation and premium gasolines because of its superior performance in gasolines having a high aromatic hydrocarbon content.

Thioalkyl lead compounds are used as anti-mildewing agents in the cotton industry. They also have various medical applications as antiinflammatory and antiandrogenic agents. Nitrogen-containing, heterocyclic, organolead compounds are known for their excellent biocidal activity (Shapiro and Frey, 1968).

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* "All surface conditions identified as immediate hazards are to be thoroughly cleaned (washed, sanded, wire-brushed, scraped or otherwise cleaned) as to remove all cracked, scaling, peeling, chipping, and loose paint on applicable surfaces. Surfaces shall then be repainted with two coats of a suitable non-leaded paint."

Further uses of various lead compounds are shown in Table 8.1 .

7.3 DISTRIBUTION OF LEAD IN THE ENVIRONMENT

As a result of the widespread use of lead and its compounds, it is ubiquitous in the environment. It will be found in all three forms--gaseous, liquid, and solid. Since man acquires his body burden from all three sources, one domain cannot be considered singly, to the exclusion of the others. Pinkerton, et al., (1974), in following up this approach, suggest that ambient air, soil, dustfall, water, and if possible, food and house dust should be included in multimedia indices of environmental trace-metal exposure in humans.

7.3.1 Distribution in Air

Natural sources of atmospheric lead are airborne dust and gases diffusing from the earth's crust. These gases include radon-222, one of the daughter products of the radioactive decay of uranium-238, which is present in varying abundance in the rocks of the earth. Being a gas it can escape from the earth's crust into the atmosphere. Radon-222 decays radioactively to form a chain of solid radioactive daughter products, the end product of which is stable lead-206. The longest-lived daughter product is lead-210 which has a half-life of approximately 20 years. Diffusion of radon-222 into the atmosphere results in the presence of lead-210 in amounts ranging from 7 x 10^{-3} disintegration per minute per kilogram of air at ground level to 10 times that amount at an altitude of 47,000 feet (Burton and Stewart, 1960). This increase with altitude can be attributed both to nuclear test explosions and diffusion effects in the atmosphere, troposphere, and stratosphere.

For the continental United States, the baseline concentration for total atmospheric lead has been suggested to be 0.0080 microgram per cubic meter (Chow, et al., 1972). This value is the annual average lead aerosol concentration measured at White Mountain, California, at a virtually uninhabited site at an elevation of 3,800 meters, far above the thermal inversion.

Patterson (1965) estimated that the contribution of lead in the atmosphere from natural sources ranges from 5 x 10^{-4} microgram per cubic meter for silicate dusts down to 2 x 10^{-9} microgram per cubic meter for meteoric sources (see Table 7.3).

By far the largest amount of lead that reaches the atmosphere results from the combustion of the tetraethyl- and tetramethylleads that are used as antiknock agents in gasolines. Averaged over 50,000 miles of driving, about 70 percent of the lead burned is exhausted as particulate matter. The combustion of leaded gasoline accounts for by far the largest portion of all lead now reaching the environment (U.S. Environmental Protection Agency, 1977).

Table 7.3 ESTIMATED AMOUNTS OF LEAD IN THE ATMOSPHERE FROM NATURAL SOURCES[a],

Source	Lead Concentration, $\mu g/m^3$
Silicate dust	5×10^{-4}
Volcanic halogen aerosols	3×10^{-5}
Volcanic silicate smoke	6×10^{-6}
Forest fire smoke	6×10^{-6}
Aerosolic sea salts	1×10^{-6}
Meteoritic and meteoric smoke	2×10^{-9}

[a] Source: Patterson, Reprinted with permission from Archives Environmental Health. (c) American Medical Association, 1965

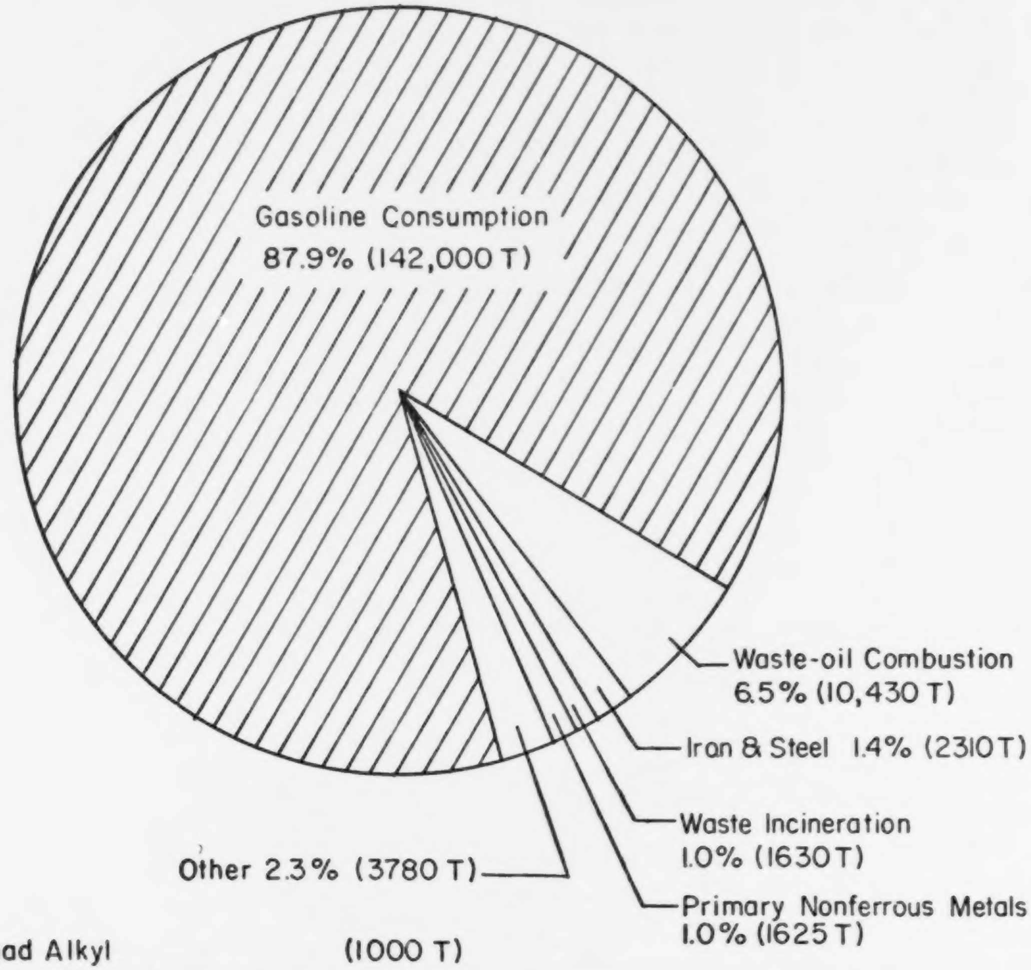
Chow and Johnstone (1965) verified that the lead in aerosols of the Los Angeles Basin, California, had the same isotopic composition as the lead in the antiknock gasoline sold in that area. In 1968, when all gasoline was leaded, about 98 percent of the atmospheric lead could be attributed to that source (National Academy of Sciences, 1972). The combustion of leaded gasoline continues to be by far the largest contributor to atmospheric lead. As of 1975, this was estimated to amount to 142,000 metric tons (U.S. Environmental Protection Agency, 1977). Additionally, some 10 percent of the lead in the gasoline accumulates in the crackcase oil; combustion of waste lubricating oil adds another 10,400 metric tons or so to that emitted from the exhaust pipe. The total of automobile antiknock-related air emissions is almost 95 percent of all emissions (Figure 7.1).

Systematic measurements of lead in the atmosphere of a city began in 1941 in Cincinnati, Ohio, but the work was interrupted by World War II and not resumed until the 1950's, at which time a number of U.S. cities were included. The 1941 data from Cincinnati gave an average lead concentration of 5.1 micrograms per cubic meter. Cholak (1964) reported that investigations in Cincinnati from 1941 to 1962 showed a continual and gradual downward trend in both mean and median concentrations of lead in air. The mean concentration of 5.1 micrograms per cubic meter in 1941 decreased to 1.43 micrograms per cubic meter in 1962 while the median level fell to 1.27 micrograms in 1962. After 1954, no concentration above 8 micrograms of lead per cubic meter of air was found. The higher average values and ranges found from 1941 to 1951 may have been partly due to the manner of sampling during this period, and therefore were somewhat biased.

Analysis of samples from 24 cities in the United States during 1954 to 1955 yielded a mean concentration ranging from 1.47 to 1.99 micrograms of lead per cubic meter, while median values ranged from 1.2 to 1.42 micrograms. Cities with a population above 2 million had significantly higher mean and median values; Los Angeles had the highest mean level of concentration (5.5) as shown in Figure 7.2.

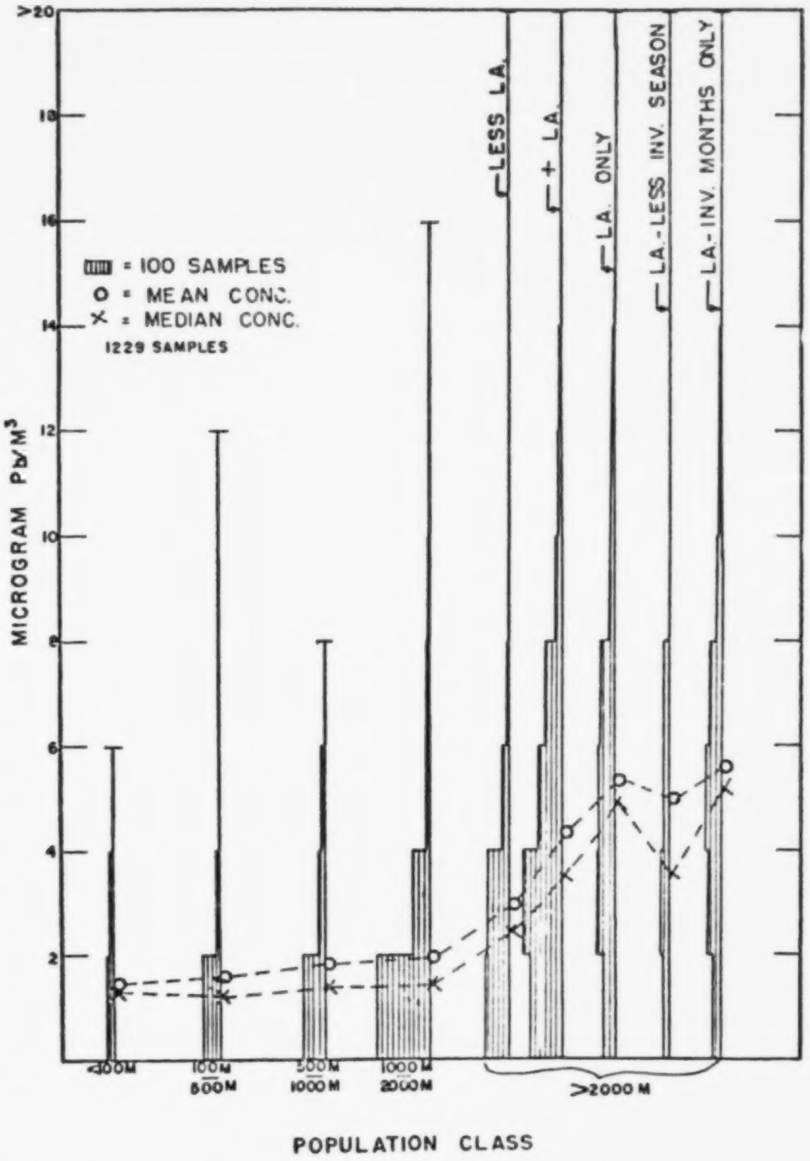
Other data indicate that lead concentration levels in the atmosphere subsequently increased, at least up to 1970, a not unreasonable phenomenon considering the increases in consumption of gasoline additives during this period. Chow (1973), in summarizing the findings of the Tri-City Project, conducted in 1961-1962 in Los Angeles, Philadelphia, and Cincinnati, and of the Seven-Cities Project, conducted in 1968-1969 in these same three cities, plus New York, Chicago, Houston, and Washington, D.C., points out that in Los Angeles the average lead concentration in the Basin increased 56 percent over this period, an annual increase of 7 percent compounded. In Philadelphia and Cincinnati, the increases were more moderate, 19 percent and 17 percent, respectively. Of the 19 sampling sites, lead concentrations increased in 17, and decreased in 2 (National Academy of Sciences, 1972).

An extensive study to determine the variation in the annual, seasonal, monthly, and diurnal average distributions of lead and total particulate matter in the atmosphere of Cincinnati, Los Angeles, and Philadelphia was carried out by continuous sampling from June 1961 through May 1962 (U.S. Department of Health, Education, and Welfare, 1965a,b). A summary of the results in Table 7.4 shows that the general urban concentrations ranged from



Lead Alkyl	(1000 T)
Secondary Lead Smelting	(755 T)
Fossil Fuel Combustion	(500 T)
Type Metal	(435 T)
Cement Mfg	(300 T)
Metallic Lead Products	(290 T)
Lead Pigments	(110 T)
Misc	(100 T)

Figure 7.1. Percent distribution of estimated emissions of lead to air, 1975, in metric tons. Data from U.S. Environmental Protection Agency (1977).



7.2 Bar graph showing ranges, means, and medians of the concentration of lead in the atmosphere of cities grouped according to population. Source: Cholak. Reprinted with permission from Archives Environmental Health. (c) American Medical Association, 1964.

Table 7.4 CONCENTRATION OF LEAD IN THE ATMOSPHERE[a]

	Atmospheric Lead Concentration, $\mu g/m^3$		
	Cincinnati	Los Angeles	Philadelphia
Annual average values			
Downtown	2	3	3
Outlying area	1	2	1
All stations	1.4	2.5	1.6
Seasonal distributions (all stations):			
Summer	1.3	1.9	1.4
Fall	1.7	2.8	1.9
Winter	1.3	3.1	1.9
Spring	1.3	2.1	1.4
Diurnal distributions (annual--all stations stated as a fraction of annual mean):			
2300-0300	1.3	1.0	0.9
0300-0700	1.1	1.1	0.8
0700-1100	1.4	1.2	1.4
1100-1500	0.8	0.7	0.8
1500-1900	0.9	0.8	1.1
1900-2300	1.0	1.1	1.1

[a] Adapted from U.S. Department of Health, Education and Welfare (1965a).

about 1 to 3 micrograms per cubic meter depending on the area sampled. The average concentration of lead for all samples collected during the year was 1.4 micrograms per cubic meter in Cincinnati, 2.5 in Los Angeles, and 1.6 in Philadelphia. The highest average concentration for all samples collected during a single month at any single sampling site was 3.1 micrograms per cubic meter in Cincinnati, 6.4 in Los Angeles, and 4.4 in Philadelphia. The highest individual concentrations were 6.4 micrograms per cubic meter in Cincinnati, 11.4 in Los Angeles, and 7.6 in Philadelphia. A uniform sampling procedure was used in each of the cities, and the samples were analyzed by the same technique.

Measurements made in Helena, Montana, during the summer and fall of 1969 showed an average daily lead concentration of 0.1 microgram per cubic meter with maximum daily levels up to 0.7 microgram per cubic meter (U.S. Environmental Protection Agency, 1972). However, in East Helena where an industrial smelter complex is located, the lead concentration averaged 0.4 to 4 micrograms per cubic meter depending on location. The maximum daily concentration observed there was 15 micrograms per cubic meter. Within a 1-mile radius of the smelter, the fallout of lead on the ground ranged from 30 to 140 milligrams per square meter; an area of 0.05 to 0.18 square meter would contain the body-burden limit for lead.

Enrichment factors which involve the ratio of metal concentrations in the atmosphere to that in the earth's crust, and which are normalized by relating to the aluminum content were determined for the Boston area by Gordon, et al., (1973). For lead an enrichment factor of 5,800 was calculated, a value significantly larger than that for any of the other 22 elements included in the study. A similar calculation made for air over the North Atlantic Ocean indicated an enrichment factor of 2,200 for lead (Duce, et al., 1975).

Chow (1973) compiled data from various parts of the world which indicate that lead concentrations may range from a low of 2×10^{-4} to 71.3 micrograms per cubic meter (Table 7.5).

7.3.2 Distribution in Water

The lead content of various surface waters of the U.S. have been reported by Kroner and Kopp (1965). Samples were taken from the Great Lakes and from five large rivers: Colorado, Columbia, Ohio, Mississippi, and Missouri. The concentration ranges found for lead were, respectively. in micrograms per liter (ppb): Ohio River, 10 to 30; Mississippi River, 10 to 50; Columbia River, 4 to 50; Great Lakes, 3 to 20. Unusual values were shown for the Mississippi River (80, 100, 200), the Great Lakes (90) and for the following (range values were not given): Colorado River (60, 600), Missouri River (20, 90). The frequency of detection, in percent, was: Ohio River, 11; Colorado River, 6; Missouri River, 3; Mississippi River, 11; Columbia River, 29; Great Lakes, 20.

In more extensive sampling of U.S. surface waters in 1970, three categories were sampled: (1) sources of public water supplies of large cities;

Table 7.5 LEAD IN THE ATMOSPHERE[a]

Conc., µg/m3	Period	Significance
0.0002		Novaya Zemlya, USSR, 1966
0.0005		Thule, Greenland, 1965
0.0006		Calculated 'natural' atmosphere
0.001		Mid-Pacific Ocean, 1967
0.004	Annual average	South Pole, 1971
0.008	Annual average	White Mountain, California, 1971
0.07	Annual average	Laguna Mountain, California, 1971
0.32	Annual average	Tashkent, USSR, 1966
0.42	Annual average	La Jolla, California, 1971
0.7	24 h average	USSR limit for general population
1.5	30-day average	California limit for general population
2.0	90-day average	US limit for general population
2.0		WHO limit
2.1	Annual average	San Diego, California, 1971
3.5	Annual average	High Street, Warwick, England, 1965-66
3.2	Daytime	Fleet Street, London, 1962
5.4	Daytime	Fleet Street, London, 1971
3.6	Annual average	Los Angeles, California, 1968-69
7.6	Monthly average	Los Angeles, California, highest 1968-69
8.1	Weekly average	San Diego, California, highest 1968
10.1	8 h per day	USSR limit for industrial exposure
25.0		Average Los Angeles freeways, 1961-62
71.3		Recorded during peak traffic in Los Angeles
200.0	8 h per day	US unofficial limit for industrial exposure, 1966

[a] Source: Chow. Reprinted with permission from Chemistry in Britain. (c) The Chemical Society, 1973.

(2) water courses downstream from major municipal and industrial complexes; and (3) U.S. Geological Survey hydrologic bench-mark stations (Durum and Hem, 1972). Analyses of 727 samples taken in various parts of the country gave lead values ranging from 1 to 890 ppb with median values from 1 to 6 ppb. As shown in Table 7.6, lead was present in almost two-thirds of the samples. The data have a regional pattern showing that lead occurred most frequently in the northeast and southeast portions of the country.

Regional studies in California covering 383 samples from miscellaneous water sources (Bradford, 1971) showed median values for lead of about the same magnitude as those presented in Table 7.6. The water sources sampled included surface waters, wells, agricultural drainage, domestic wastes, metal and chemical processing plant effluents, rivers, bays, and oil well brines. In general, the mean values for lead were only slightly higher than the medians, indicating that extremes did not have much influence on the averages. An exception to this was the category of domestic wastewaters which had a mean of 34 ppb as compared to a median of 10. One extreme value of 2,000 ppb was encountered in a processing plant effluent.

Another regional study involving Champaign County, Illinois, consisted of monitoring two streams, one draining an agricultural area and the other draining the cities of Champaign and Urbana (Rolfe and Edgington, 1973). Suspended solids were removed with a 5-micrometer filter, and were analyzed separately from the liquid fraction. The concentration of dissolved lead generally ranged from 0 to 15 ppb while that in the suspended solids was significantly higher and varied a great deal. In the urban drainage, lead in the suspended solids ranged from 2 to 29 times as much as that in the liquid fraction. For the rural area, lead content ranged from equal amounts to 5 times as much. The larger amount from urban sources was attributed to lead particulate being deposited on paved city streets and being washed off by rains.

Other comparisons of the soluble lead and lead in particulate matter have been made for Cayuga Lake, New York, and its tributaries. Soluble lead was present in the lake at an average concentration of 0.12 ppb while it averaged 0.91 ppb in the tributary streams (Mills and Oglesby, 1971; Kubota, et al., 1974). Lead in the particulate matter that was filtered from the streams was reported as averaging 2.06 ppb. Particulate lead was concluded to be a better indicator of the impact of urbanization than soluble lead, which did not show much difference between streams flowing through rural and urban areas.

Similar data were collected for two streams in Tennesse, of which one was chosen because it lies near mineral outcrops which would provide metal content to the water (Perhac, 1972). A considerably higher lead content was measured in these streams which averaged 15 ppb. The water samples were divided into three fractions by ultracentrifugation: coarse particulate, colloidal, and dissolved solids. The highest lead concentration was found in the colloids from three of the four samples as shown in Table 7.7. The lowest concentrations were in the dissolved solids with the coarse particulates in between. However, because the amount of insoluble material in the

Table 7.6 REGIONAL SUMMARY OF LEAD IN SURFACE WATERS OF THE U.S.[a]

Region	Lead Concentration, ppb Maximum	 Minimum	 Median	Not Detected Percent	Detected Percent
New England and Northwest	890	1	6	8	92
Southeast	44	1	4	27	73
Central	84	1	1	51	49
Southwest	34	1	1	61	39
Northwest	23	1	1	62	38

[a] Source: Durum and Hem. Reprinted, with permission, from Annals of New York Academy of Science. (c) New York Academy of Science. (1972).

Table 7.7 DISTRIBUTION OF LEAD IN DISSOLVED AND SUSPENDED SOLIDS OF TWO TENNESSEE STREAMS[a]

	Lead Concentration, ppm				Percentage of Total Lead			
Sample No.	1	2	3	4	1	2	3	4
Dissolved solid	77	75	84	96	95.0	90.9	87.9	89.5
Coarse particulate	124	213	653	123	5.0	7.6	9.3	10.1
Colloid	62	2820	2820	<850	Trace	1.5	2.8	0.4

[a] Source: Durum and Hem. Reprinted, with permission, from Annals of New York Academy of Science. (c) New York Academy of Science. (1972).

streams was relatively small, most of the total lead was contained in the dissolved solids portion. Sample 1 was taken upstream of the mineralization of one stream and showed the lowest lead concentration. Samples 2 and 3 were taken in the same stream but below the mineralization. The marked enrichment of lead in the colloidal fraction suggests that adsorption by small particles may be a significant mechanism in the transport of lead in water.

Although the air and soil in the East Helena, Montana, contain more lead than the national average because of the presence of a smelter, the water in the area did not show excess levels of lead. Concentrations from 1 to 40 ppb were found in the Helena area which are no greater than those found in other parts of the country (U.S. Environmental Protection Agency, 1972).

Water in areas in which lead has been mined can be expected to have greater than average amounts of lead. The Springfield region of Missouri which has been mined for lead was surveyed by Proctor, et al., (1973) for the lead content of surface waters and wells. In some localized areas the lead content of the drinking water exceeded the acceptable PHS limit of 50 micrograms per liter. However, most water samples had a lead content below this limit. As shown in Table 7.8, seasonal variations occurred, and surface waters contained the most lead in fall and winter whereas well waters showed greater lead content during the wet summer period.

The lead profiles in the major oceans of the world were determined by Chow (1968) who used mass spectrometric techniques to analyze samples from various depths as well as locations. The results, which are shown in Figure 7.3, indicate that there are no essential differences in lead concentrations in deep waters below the 1,000-meter level. In the surface layers, however, lead is present in greater amounts in the Pacific and Mediterranean waters than in the central Atlantic which is away from land influences. Chow also cited data by other investigators (see Table 7.9) which show that values found in different places ranged from 0.02 microgram per kilogram in ocean depths to 8 micrograms per kilogram in surface waters off Europe. According to Goldberg (1971) about 250,000 metric tons of lead are annually washed out over the oceans and about 100,000 metric tons over the continents in correspondence to their relative areas.

In a survey of water pollution control in the primary nonferrous metals industry made for EPA by Battelle-Columbus Laboratories (Hallowell, et al., 1973), effluents from the tailings ponds were reported to contain anywhere from no lead to 800 ppb. The combined process and cooling waters from lead smelters and refineries which were released into streams contained from 70 to 157 ppb of lead. The streams into which the wastes were released originally contained from 0 to 50 ppb, as measured at points considered unaffected by plant effluents.

The contribution of lead pipes to the level of lead in drinking water can be significant. In a recently completed study for EPA, a Tufts University group found that Boston City water contains 25.5 percent more lead than the federally permissible level of 50 ppb (Anon., 1975). The high lead content

Table 7.8 LEAD CONTENT OF THE WATERS OF THE SPRINGFIELD AREA, MISSOURI[a]

Water	Seasons[b]	Concentration, ppb			
		Mean	Max.	Min.	Standard Deviation
Surface	1	6.47	70	0	12.63
	2	2.8	5.7	0.5	1.5
	3	0.17	1	0	0.36
Shallow wells (<500 ft)	1	3.03	11.25	0.75	2.94
	2	5	15	1	3.55
	3	2.94	32	0	8.15
Deep wells (>500 ft)	1	1.51	6.25	0.01	1.69
	2	2.67	8	0	2.41
	3	2.45	12	0	3.97

[a] Source: Proctor, et al. Reprinted with permission from Proceedings 7th Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1973.

[b] 1 = fall and winter, dry.
2 = spring, dry.
3 = later summer, very wet.

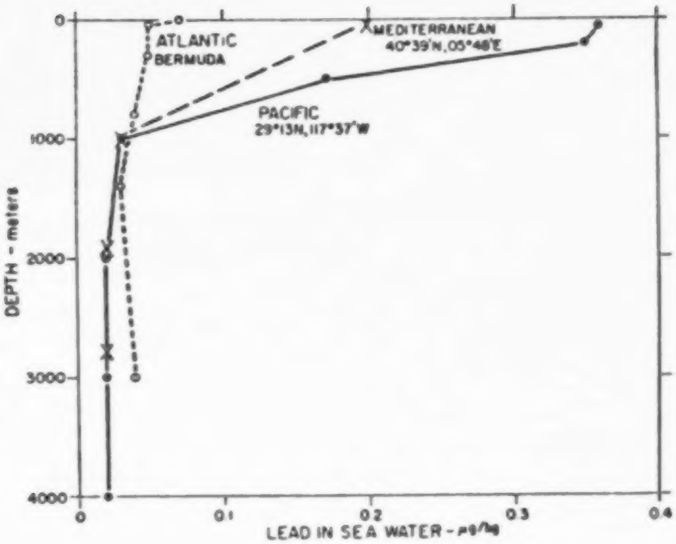


Figure 7.3 Lead profiles in the major oceans. Source: Chow. Reprinted with permission from Journal of Water Pollution Control Federation. (c) Water Pollution Control Federation, 1968.

TABLE 7.9 LEAD CONTENT OF VARIOUS MARINE WATERS[a]

Source of Seawater	Concentration ppb
Florida Key	3-5[b]
North Sea--Surface	2
Brittany-Surface	3-8
Gullmarfjord-Surface	5-8
Japan Coast-Surface	4
English Channel-Surface	5
Washington Coast-to 100 m	0.1
English Channel	0.6 -1.5
Atlantic-to 5,300 m	0.02-0.10
Pacific-to 4,000 m	0.02-0.35
Bermuda-to 3,000 m	0.03-0.07

[a] Source: Chow. Reprinted with permission from Journal of Water Pollution Control Federation. (c) Water Pollution Control Federation, 1968.

[b] Limit of sensitivity of method.

was attributed to the acidity of the city water which is sufficient to corrode old lead pipes in the water supply system. Boston water supplies come from watersheds lying to the north where the rock is igneous rather than sedimentary, so that the water composition falls in the small select group in the U.S. with very low dissolved solids. Thus, the City of Boston has soft, low pH water and an old piping system in which lead water pipes are still in use, a combination known to cause excessive dissolution of lead. It is planned to adjust the pH to reduce the corrosion of the old lead pipes; 2,000 metric tons (2,200 tons) of sodium hydroxide will be required annually to accomplish this (Anon., 1975).

Glasgow, Scotland, is one of the largest soft water areas in the United Kingdom, and is an old city in which there are a number of houses which contain not only lead pipes, but also lead water storage tanks (one nearly 200 years old). Not surprisingly, some amazing lead concentrations (up to 2,000 to 3,000 ppb) were observed in the domestic water supplies of some homes (Goldberg, 1974). The results of the study by Goldberg underline the possible danger to health of lead plumbing in a soft water area such as Glasgow.

Investigations were carried out on the clinical and metabolic effects of lead acquired by drinking soft domestic water from lead plumbing systems in 23 households (71 inhabitants). Three groups were studied: Group 1, comprising families whose house had a lead-lined tank for storage of drinking water plus lead piping; Group 2, where there was no lead tank but lead piping in excess of 18 meters (60 feet), Group 3, where there was less than 18 meters of lead piping carrying the drinking water supply. The results are shown in Figures 7.4 and 7.5. The lead content of water from cold water taps was up to eighteen times the upper acceptable limit and was proportional to the amount of lead in the plumbing system. The blood lead of 71 inhabitants of these houses showed a significant positive correlation with water lead content. Delta-aminolevulinic acid dehydratase activity, an extremely sensitive indicator of lead exposure, showed a significant negative correlation with water-lead content. Atmospheric lead was within acceptable limits in all but one house and no significant correlation could be found with biochemical measurements. A small number of clinical abnormalities were found but could not be directly attributed to lead toxicity.

Addis and Moore (1974) also investigated the possible environmental hazard from lead plumbing in a soft water area such as Glasgow. For their studies, the houses were divided into two groups; those less than 20 years old (Group A) and those more than 20 years old (Group B). This division was chosen because before 1939 these houses were constructed with lead plumbing and until 1967 lead link pipes were used to connect the domestic copper system to the cast iron main. Table 7.10 contains the results of their investigation. The mean lead level of the water in the Group B houses was about 350 ppb; in 82 percent of the houses in this group the lead concentration in the water was greater than 100 ppb (the WHO acceptable limit). Associated with this increase in water lead levels was a significant 1.5-fold elevation of blood lead in the occupants of older houses. When the water lead (PbW) and the blood lead (PbB) levels were compared for all subjects in the study, a significant linear regression was found with regression coefficient

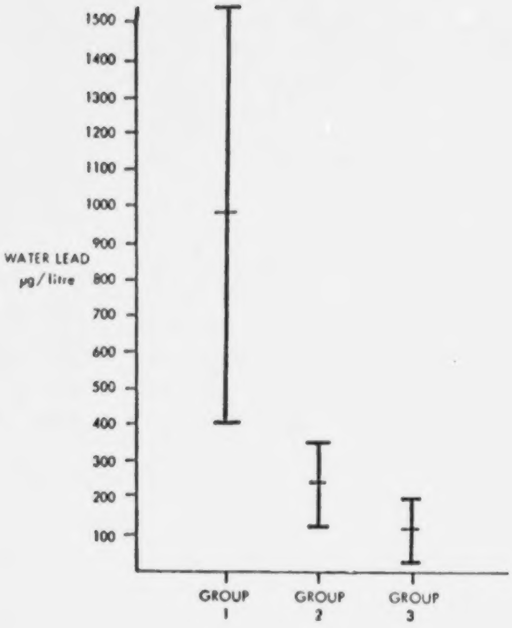


Figure 7.4 Lead content of cold tap water from three groups of Glasgow houses

Source: Goldberg (1974). Reprinted from Environmental Health Perspectives.

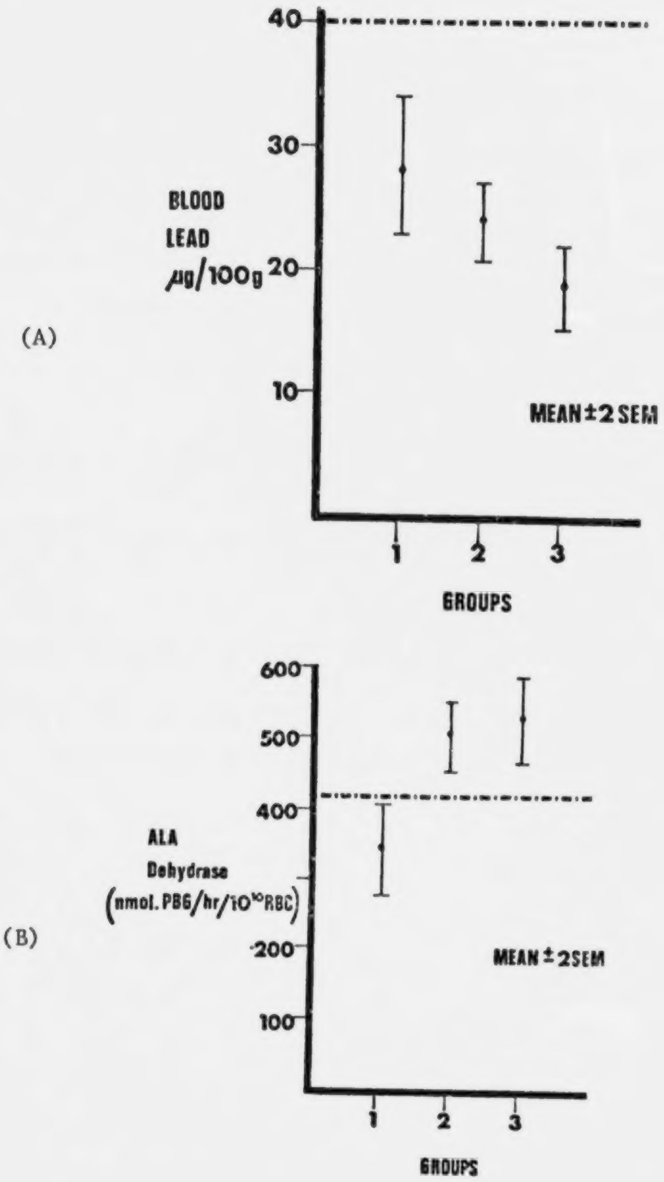


Figure 7.5 Lead pollution in Glasgow. (A) Blood levels of inhabitants of houses in the three groups. (B) Erythrocyte ALA dehydratase levels of the inhabitants of the houses of the three groups. Adapted from Goldberg (1974). Reprinted from Environmental Health Perspectives.

Table 7.10 LEAD IN GLASGOW WATER[a]

	Group A (<20 yr)	Group B (>20 yr)	Significance
No. in group	12	38	
Mean age of house	13.5 ± 4.4	42.6 ± 4.2	--
Time of residence	8.8 ± 5.3	16.1 ± 12.5	NS[b]
Age of resident	41.3 ± 18.8	46.7 ± 17.8	NS
Sex ratio (female:male)	2 : 1	29 : 9	--
Water lead (ppb)	34.6 ± 29.5	353.1 ± 255.6	P<0.001
Blood lead (μg/100 ml)	19.8 ± 8.4	30.5 ± 10.6	P<0.01
δ-aminolaevulinic acid dehydratase (units)	27.8 ± 13.2	22.3 ± 10.4	NS
ALAD			
Residence>5 yr (No. of subjects)	30.4 ± 12.9(10)	18.9 ± 5.1(30)	P<0.005

[a] Source: Addis and Moore. Reprinted with permission from Nature. (c) Macmillan, Ltd. (1974).

[b] Not significant.

$r = 0.417$ using the Equation $PbB = 0.018\ PbW + 22.9$.

Of particular interest was the observation that for all residents in the survey, there was a significant negative exponential regression relationship between erythrocyte ALAD activities and water lead levels, using the equation $ALAD = 25.7e^{-0.0006\ PbW}$

7.3.3 Distribution in Soil and Rock

The earlier work on measurement of lead in soils and rocks has been summarized by de Treville (1964) who reported data which were compiled mainly at the Kettering Laboratory. These data indicate that an average value for the earth's crust is 16 ppm with alkaline rocks contributing about 8 ppm and acidic rocks about 20 ppm. Alluvial soil gave values as low as 0.04 ppm, while agricultural soil in New Jersey contained as much as 95.7 ppm. In old residential sections of cities where lead paints were used for many years, values as high as 360 ppm were found. In the vicinity of lead ores the soil was reported to have up to 10,000 ppm of lead.

In more recent work, Connor, et al., (1971) examined the effect of roadside location on the lead content of rocks, subsurface soils, and vegetation. The analyses showed the general trend of "on-road" samples of vegetation containing more lead than the "off-road" samples. However, none of the three rock types (limestone, shale, and sandstone) sampled showed any accumulation of lead in the "on-road" samples. In fact, shale showed the opposite effect which was attributed to geological origins. Connor, et al., were unable to demonstrate any effect of distance from the road for soil taken a few centimeters below the surface. Zimdahl (1971, 1972) reported that for certain samples of Colorado roadside soils lead concentrations decreased from 1,040 ppm at the surface to 250 ppm at a depth of 13-15 cm (5 to 6 in.).

Comparison of the lead content of urban soils in a region which included industrial, agricultural, and residential areas showed that there was about 2.7 times as much lead in industrial soil as in residential soil (Klein, 1972). The agricultural soils contained slightly less lead than those in residential areas.

A very high lead concentration was found near a heavily-traveled expressway in Chicago. The soil contained as much as 7,600 ppm at distances up to 13.7 meters from the expressway, and 900 ppm up to 45.7 meters (Khan, et al., 1973). The amount of lead varied with the seasons in a fashion similar to the seasonal variations in average monthly traffic volumes on the expressway. Lead levels were lowest during fall and winter, increased during spring, and reached their highest values during the summer.

The accumulation of lead in soils over a period of about 40 years was compared for areas of high and low motor vehicle traffic densities in the Los Angeles area (Page and Ganje, 1970). The sampling sites were more than 1.6 kilometers from any major highway. No lead accumulations as a function of time were observed where motor vehicle traffic was less than 80 vehicles per 2.6 square kilometers (square mile). In areas where the traffic density exceeded 580 vehicles per 2.6 square kilometers, the surface concentration of lead (2.5-cm depth) increased by a factor of 2 to 3, which amounted to an accumulation of 15 to 36 ppm of lead. The highest value recorded for any of the locations was 52 ppm.

Lagerwerff and Specht (1970) present data typical of the depth profiles for lead found by various investigators. Table 7.11 summarizes the results, and shows about a 65 to 75 percent reduction in lead content in the top 5 centimeters of soil for samples taken at points 8 to 32 meters from a highway. In every case the amount of lead decreased with depth of sample.

The presence of a lead smelter can cause very high lead levels in nearby soils. In the Helena, Montana, study cited previously, the upper 2.54 centimeters of uncultivated soil were found to contain 4,000, 600, and 100 ppm of lead at distances from the smelter of 1.6, 3.2, and 6.4 kilometers (1, 2, and 4 miles), respectively (U.S. Environmental Protection Agency, 1972).

Roberts, et al., (1974) found that a high rate of lead fallout around two secondary lead smelters originated mainly from large-particulate emissions from low level fugitive sources rather than from stack fumes. The lead content of dustfall, and consequently, of soil, vegetation, and outdoor dust, decreased exponentially with distance from the two smelters. Lead emissions from the two smelters were estimated to be 15,000 to 30,000 kilograms per year. Regression analysis of the concentrations indicated an exponential decrease with distance, from values of 40,000 and 16,000 micrograms per gram of soil close to smelter A and smelter B, respectively, to an urban background of 100 to 500 micrograms per gram of soil, which accounted for 60 to 80 percent of the variability in data. Although the monthly geometric means of the lead concentration in particles close to the smelters (1 to 5.3 micrograms per cubic meter of air) were only double those for urban sites (0.8 to 2.4 micrograms per cubic meter) the range of the daily concentrations was much greater, producing a marked log normal distribution.

Hemphill, et al., (1974) studied roadside lead contamination in soils along highways used for transport of lead concentrate in the Missouri lead belt. As shown in Table 7.12, lead values approaching 3,800 micrograms per gram (ppm) of dry weight were found at zero distance from the road. Along control routes high lead values of 384 micrograms per gram of dry weight were observed. The total lead in soils decreased rapidly at 100 to 300 meters. The investigators suggested that the elevated levels of lead in the soil near the control routes are probably due to contamination from motor fuel and possibly other sources.

The use of lead paints on the exterior of houses has been found to result in locally high concentrations of lead in soils. Soil samples taken near old houses in Cincinnati built prior to 1900 had lead concentrations which ranged from 32.5 to 7,620 ppm. In general there was a correlation between soil lead, and the lead content of the exterior paint on the houses (Bertinuson and Clark, 1973). This work also demonstrated that much more

Table 7.11 LEAD CONTENT IN ROADSIDE SOIL AND GRASS AS A FUNCTION OF DISTANCE FROM TRAFFIC AND SOIL DEPTH[a]

Site	Distance from Road, m	Lead Content, μg/g dry weight			
		Grass	Soil Profile Layer, 0–5 cm	Soil Profile Layer, 5–10 cm	Soil Profile Layer, 10–15 cm
I West of U.S. 1, near Plant Industry Station, Beltsville, Maryland	8	68.2	522	460	416
	16	47.5	378	260	104
	32	26.3	164	108	69
II West of southbound lanes, Washington-Baltimore Parkway, Bladensburg, Maryland	8	51.3	540	300	98
	16	30.0	202	105	60
	32	18.5	140	60	38
III West of Interstate 29, Platte City, Missouri	8	21.3	242	112	95
	16	12.5	140	104	66
	32	7.5	61	55	60
IV North of Seymour Road, Cincinnati, Ohio	8	31.3	150	29	11
	16	26.0	101	14	8.2
	32	7.6	55	10	6.1

[a] Source: Lagerwerff and Specht. Reprinted with permission from Environmental Science and Technology. (c) American Chemical Society.

TABLE 7.12 TOTAL LEAD IN SOILS OF THE MISSOURI LEAD BELT[a]

Distance From Road Right-of-Way, m (yd)		Lead, µg/gm Dry Weight[b]			No. of Samples
		Low	Mean	High	
			Ore Truck Routes		
0	0	16.7	809.6	3,792.0	56
91	(100)	12.7	32.5	80.0	28
183	(200)	20.0	36.0	48.0	11
274	(300)	33.0	52.0	55.0	5
			Control Routes		
	0	10.7	75.6	384.0	24
91	(100)	9.3	23.2	49.0	16
183	(200)	8.3	17.3	27.0	9
274	(300)	13.3	17.3	20.0	5

[a] Source: Hemphill, et al. Reprinted with permission from Archives Environmental Health. (c) American Medical Association, 1974.

[b] In 1 to 6-inch zone.

lead could be accumulated in the soil around a house with lead paint than at the roadside where heavy automobile traffic passed (10,200 vehicles per day). The house contribution to soil lead was about 30 times greater than that from the road. This source of lead can be accentuated if the old paint is chipped and scraped from the wood and then allowed to disperse in the vicinity. One such measurement showed that lead in the soil 15 to 30 meters from the house was 165 to 185 ppm when the old paint was removed. A year later the lead content had increased to 440 to 490 ppm (Bogden and Louria, 1975).

It has long been recognized that the eating of leaded paint is a main cause of lead poisoning and elevated blood leads of children living in dilapidated housing. In this connection, Ter Haar and Aronow (1974) determined the source of lead in dirt to which children are normally exposed. Dirt samples were taken in old urban areas around 18 painted frame houses and 18 houses of brick construction (Table 7.13). The data suggested that (1) weathered lead-based paint is a major contributor to soil lead, and (2) vehicular sources probably make a significant contribution to soil lead near the sidewalks.

High local concentrations of lead might be expected to occur in soils where plants and trees have been sprayed with lead arsenate. In past years this compound was used as an insecticide but has been presently supplanted by organic compounds. However, the soil of an orchard which had been sprayed with lead arsenate for many years was found to contain about 50 to 65 ppm of lead. This is not an unusually high value; however, it is significantly greater than the 15 to 20 ppm which is typical of uncontaminated areas (Vandecaveye, et al., 1936).

7.4 ENVIRONMENTAL FATE OF LEAD

7.4.1 Mobility and Persistence in Air

The physical form of lead in the atmosphere is important to its subsequent disposition. Large particles will fall out near the emission source while the smallest particles will persist for relatively long times. Aerosol lead may be emitted to the atmosphere in the form of dust, fume, mist or vapor depending on the source and the method of generation. Dusts are the larger particles (1 to 150 micrometers in diameter) that result from mechanical processes such as grinding. Fumes range in size from 0.12 to 1 micrometer and result from chemical processes. Mists result from condensation of vapors on submicroscopic dust particles, and vapors are evaporated liquids.

The particle size distribution of lead aerosols in several large cities was found by Robinson and Ludwig (1967) to have a fairly wide range. Measurements made at 59 sites in Los Angeles, San Francisco, Cincinnati, and Chicago gave a mass median equivalent diameter (MMED) of 0.25 micrometer with 25 percent of the particles smaller than 0.16 micrometer, and 25 percent larger than 0.43 micrometer. Lee, et al., (1968) found a MMED of 0.18 micrometer for lead aerosols in Cincinnati and 0.42 micrometer in a suburb. In this

TABLE 7.13 LEAD IN DIRT IN DETROIT[a]

	Lead Concentration, ppm			
	Painted Frame Houses		Brick Houses	
Location	Mean	Range	Mean	Range
Within 0.6 m of house				
front	2349	(126-17590)	351	(78-1030)
back	1586	(162-4951)	501	(72-2350)
sides	2257	(140-7284)	426	(91-1160)
	1846	(104-7000)	595	(40-2290)
3 m from house				
front	447	(58-1530)	156	(39-316)
back	425	(149-1410)	200	(72-480)
Near sidewalk	627	(152-1958)	324	(86-1130)
curb	572	(320-1957)	612	(147-2420)
Gutter	966	(415-1827)	1213	(304-3170)

[a] Adopted from Ter Haar and Aronow (1974).

case, 75 percent of the aerosols were less than 1 micrometer. Other work in California (Mueller, 1970) indicated that 50 to 90 percent of the lead particles in the urban air are smaller than 1 micrometer. In a later study, Lee, et al., (1972) reported atmospheric lead particle mass median equivalent diameters ranging from 0.42-0.69 micrometers in six U.S. cities.

Very large lead particulates ranging in size from 300 to 3,000 micrometers in diameter were discovered to have "fallen out" of automobile exhaust(s) within 4.9 to 6.1 meters (16 to 20 feet) of the car (Habibi, 1970). More than 95 weight percent of this lead was present as coarse particles, and the total quantity amounted to 10 percent of the lead originally contained in the gasoline consumed.

The chemical form of lead in automobile exhausts changes rather rapidly as the components react with moisture, carbon dioxide, and sulfur dioxide in the atmosphere. PbBrCl is the principal, initial component although there is evidence that exhaust particles are bromine-rich compared to stoichiometric PbBrCl (Boyer and Laitinen, 1975). Measurements made by Ter Haar and Bayard (1971) showed that the amount of $(PbO)_2$ PbBrCl in the exhaust is almost as great as that of PbBrCl. These two compounds accounted for 31.4 and 32.0 percent of the lead, respectively. Other halogen compounds and their percentages were: $PbCl_2$ (10.4), PbOHCl (7.7), $PbBr_2$ (5.5), $(PbO)_2$ $PbCl_2$ (5.2), PbOHBr (2.2), and $(PbO)_2$ $PbBr_2$ (1.1). The nonhalogen compounds found were: PbO_x (2.2), $PbCO_3$ (1.2), $(PbO)_2$ $PbCO_3$ (1.0), and $PbSO_4$ (0.1). After 18 hours, measurements showed that about 75 percent of the bromide and 30 to 40 percent of the chloride compounds had disappeared. The lead oxides, carbonate, and oxycarbonate then constituted 65 percent of the sample. On longer exposure to the atmosphere the carbonate content increased and some of the lead was converted to sulfate. Particulate samples collected in the vicinity of a rural road which would represent "aged exhaust" had a lead distribution of $PbCO_3$ (30.2), $(PbO)_2$ $PbCO_3$ (27.5), PbO_x (20.5), PbO-$PbSO_4$ (5.0), and $PbSO_4$ (3.2). The remaining 13 percent of the lead was distributed among the chloride and bromide compounds. Consequently, by the time lead aerosols are removed from the atmosphere, they are converted almost completely to carbonates and sulfates.

The presence of alkyl lead vapors (from gasoline) in ambient air has been reported by several investigators. Purdue, et al., (1973) in a study on organic lead concentration in an underground parking garage, and in general ambient air of six major U.S. cities, found that in the parking garage, lead was 11.7 micrograms per cubic meter, of which 16.7 percent was organic lead. However, in the six major cities the organic lead concentration was lower (about 10 percent) relative to the total lead. Since the concentrations of organic lead found approached the detection limit of the method, there is some uncertainty concerning the accuracy of the data. Snyder, et al., (1967), in a study in Los Angeles found that about 2 percent of the lead was organic. Differences in the concentration of organic lead found relative to particulate lead might be attributed to differences in proximity to the lead source. Uniformly low levels (under 10 percent of the total lead), except for two brief periods were reported by Laveskog (1971) who studied the presence of lead in the air at several locations in

Stockholm. These low levels occurred near a gasoline station and were attributed to evaporation of fuel spills. Colwill and Hickman (1973) confirmed Laveskog's concept. Harrison, et al., (1975a) found that organic lead levels ranged from 0.02 microgram per cubic meter in a tunnel to 0.59 microgram per cubic meter six meters from a gasoline pump.

The mass balance for automobile-related lead was developed for the Los Angeles basin by Huntzicker, et al., (1975). Lead calculated to be attributable to automobile exhaust was estimated to be 17.6 plus or minus 2.6 metric tons per day. In addition to the exhaust components, the evaporation of antiknock compounds was considered since tetramethyllead has a vapor pressure of 24 torr at 20 C and tetraethyllead, 0.15 torr (Schwarzbach, 1973). However, the contribution estimated for evaporation of antiknock compounds amounted to only 0.3 ton per day. The total amount of lead thus generated was considered to be spread over the region. Deposition near the source accounted for 9.5 plus or minus 2.2 tons per day; deposition far from the source amounted to 2.0 plus or minus 1.0 tons per day, and lead removed by wind was 5.6 plus or minus 3.0 tons per day. Essentially all of the auto-related lead (17.1 plus or minus 3.9 metric tons per day) could be accounted for in terms of these mechanisms.

The movement of particulate lead compounds was monitored along a heavily traveled freeway in Cincinnati, at a nearby park, and in a residential area about 3.2 kilometers (2 miles) away (Cholak, et al., 1968). The findings indicated an average concentration of 7.8 micrograms per cubic meter at the freeway, 1.7 at the park site, and 1.1 at the residential site, both leeward of the source of lead. The concentration of lead in the air at the latter site was approximately the same as that of 6 years previously. Concentrations of lead at the freeway site did not vary with the seasons and most likely reflected the uniformity of vehicular traffic on the roadway. At both of the other stations, concentrations were higher during the summer and fall months than during the winter and spring months. The mass median equivalent diameter of the lead particles was found to be approximately 0.30 micrometer with 70 percent of the lead particles being less than 1 micrometer. The size data indicated that most of the lead in dusts removed from the air by filtration is mainly in the size range considered "respirable". Not all of the small lead particles in the atmosphere can be attributed to automobiles, however, because emissions from a coal-burning power plant have been found to contain lead (3 percent) in the finer particles that are not collected even by a high efficiency electrostatic precipitator (Klein, et al., 1975).

Concentrations of dustfall at the three Cincinnati stations varied from 16.5 metric tons per square kilometer (47 tons per square mile) at the highway to 8.4 metric tons per square kilometer (24 tons per square mile) at the other two stations. Concentrations of lead in the dustfall at the freeway averaged 0.51 percent while at the other two stations they were only 0.12 percent. Thus, the average monthly quantity of lead at the freeway was approximately twice that at the other two sites, a main factor in the contamination of soil and vegetation near the highway (Cholak, et al., 1968). Data on concentration of lead in soils and grass roots and blades showed variations according to the distance from the roadway with most of the contamination occurring within 30.4 meters (100 feet). The top 0.63 centimeter (0.25 inch) of soil contained the highest concentration of lead which suggests surface contamination due to partial washout of lead from the atmosphere, but principally from the settling of the larger lead particles generated at the roadway.

In a study carried out in 1968 by EPA, 77 cities in the central U.S. were monitored for lead and other metals in dustfall from the atmosphere (Hunt, et al., 1971). Residential, commercial, and industrial areas were distinguished. As shown in Figure 7.6, the fallout of lead was highest in industrial areas, followed closely by commercial areas. Residential fallout was about one-half of industrial fallout. The monthly variation was not considered statistically significant.

A model for short range environmental transport and accumulation of automotive lead near open highways was developed by Vaitkus, et al., (1973). Atmospheric transport of lead from a highway (Interstate-25 in Colorado) and its removal from the atmosphere by gravitational settling, washout, and rainout were coupled with migration and retention in soil. Figures 7.7 to 7.9 show the values calculated from the model for the various ways of removing atmospheric lead. The model was found to predict lead levels reasonably well over the downwind distance to 60 meters, but was low beyond that distance (see Figure 7.10).

Kleinman, et al., (1973) computed a dispersion factor for trace metals in the atmosphere which was defined as the product of the morning mixing height and the surface wind speed. Measurements of lead and several other metals made at various locations in New York City during 1972 showed a marked seasonal variation involving a spring minimum and a summer maximum. Values for lead (see Figure 7.11) ranged from a minimum about 1 microgram per cubic meter in spring to a maximum of 4 micrograms per cubic meter in summer. The correlation between the dispersion factor and the lead concentration was highly significant at the 95 percent level. By measuring the concentration of lead-212 in vertical profiles at the Empire State Building, New York City, Assaf and Biscaye (1972) estimated that the residence time of air within the street layer was of the order of 5 minutes.

Rainfall removes lead from the atmosphere. The residence time of lead-210 in rainwater was calculated by Burton and Stewart (1960) to be 22 days for particles whose whole airborne life is spent in the troposphere. However, Francis, et al., (1970) found a residence time of only 9.6 days for filtered rainwater samples and attributed Burton's higher value to a significant dust component in the sample.

Snow is also effective in removing lead from the atmosphere. Hamilton and Miller (1971) found an average lead concentration of 410 ppb, and a maximum value of 1,090 ppb in snow collected in Columbus, Ohio. No rain data are provided for a direct comparison to precipitation as rain. A study of the lead concentration in snow in Ottawa, Ontario, was undertaken to assess the effects of snow disposal practices. One hundred and forty-nine

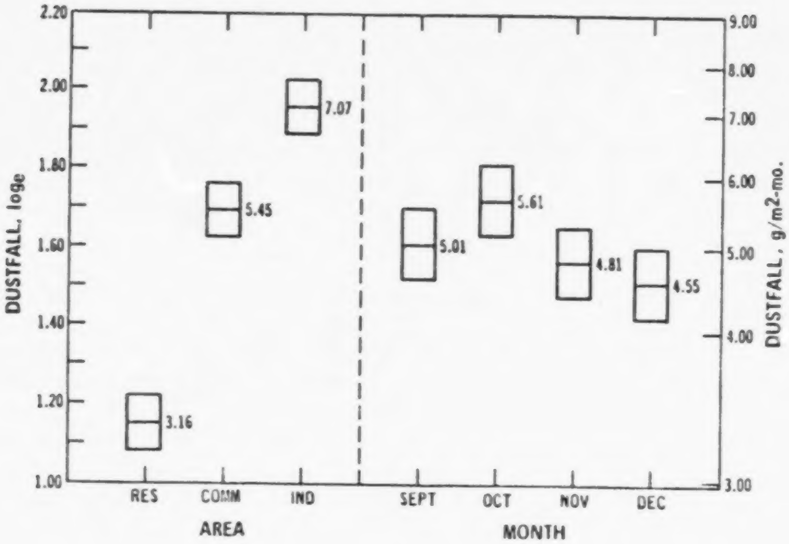


Figure 7.6 Geometric means and 95 percent confidence intervals for lead fallout measurements in 77 cities by area and month. Source: Hunt et al. Reprinted with permission from Proceedings 4th Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri. 1971.

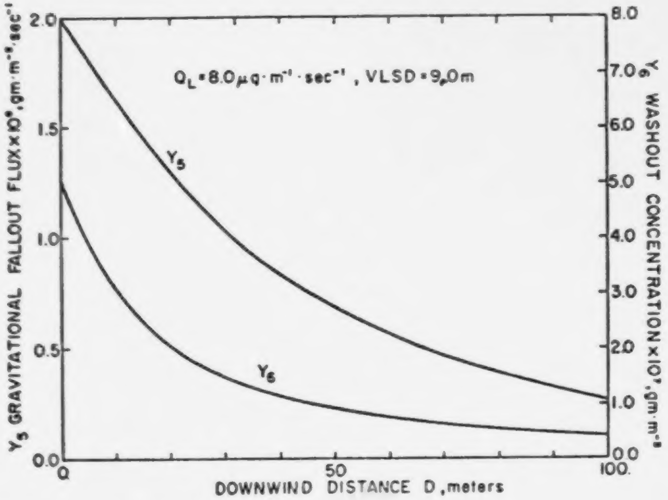


Figure 7.7 Gravitational fallout flux of lead and washout lead concentration as a function of downwind distance from edge of highway at T = 1000 sec.

[a] Source: Vaitkus, et al. Reprinted with permission from Proceedings 7th Annual Conference on Trace Substances in Envrionmental Health. (c) University of Missouri, 1973.

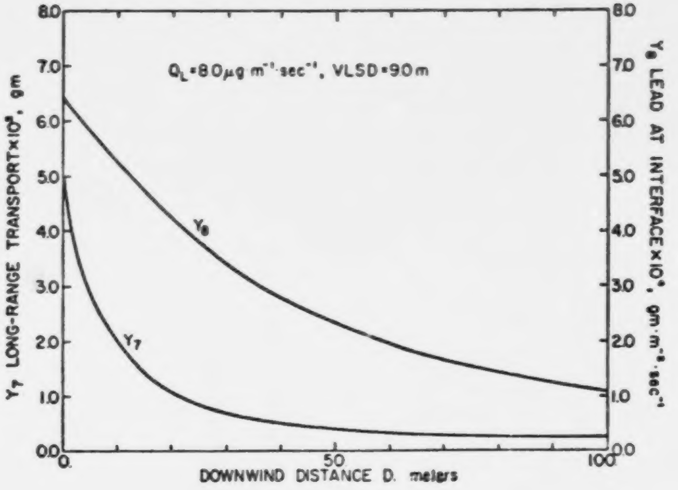
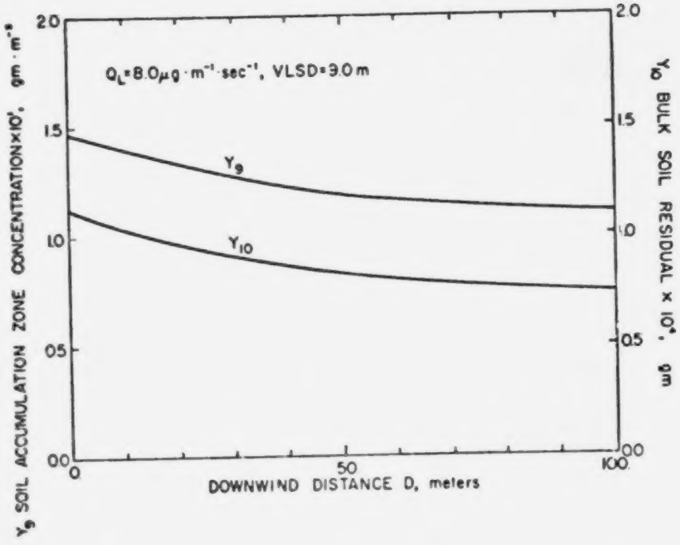
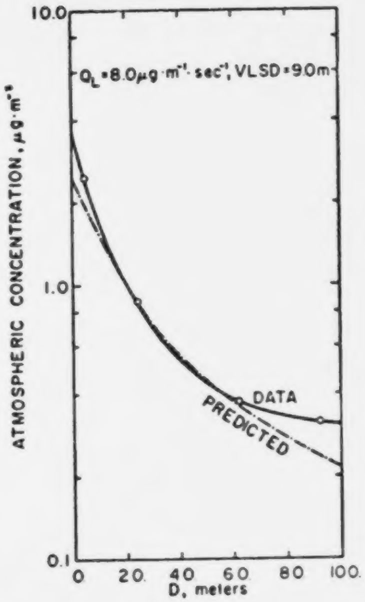


Figure 7.8 Long-range transport of lead and lead deposited at soil/air interface as a function of downwind distance from edge of highway at T = 1000 sec.

[a] Source: Vaitkus, et al. Reprinted with permission from Proceedings 7th Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1973.



7.9 Concentration of lead in soil accumulation zone and bulk soil residual lead content as a function of downwind distance from edge of highway at T = 1000 sec.



7.10 Comparison of predicated atmospheric lead concentration and measured values on Interstate 25 as a function of downwind distance from edge of highway at z = 1.2 meters.

Source: Vaitkus, et al. Reprinted with permission from Proceedings of 7th Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1973.

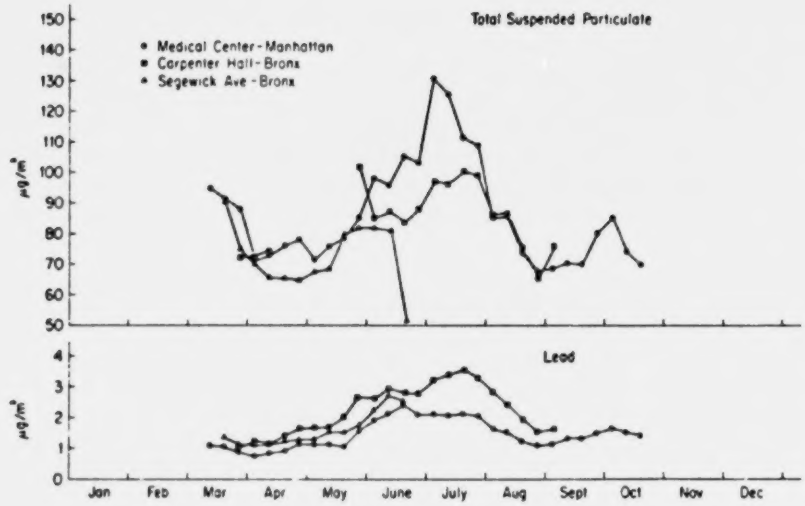


Figure 7.11 Concentrations of total suspended particulate and lead in New York City air. Source: Kleinman, et al. Reprinted with Permission from Proceedings 7th Annual Conference on Trace Substances in Environmental Health. (c) University of Missouri, 1973.

samples from eleven snow dumps within the city gave widely ranging values of 20 to 50,000 ppb, with an average of 4,800 (La Barre, et al., 1973). It is of particular significance that the runoff from these snow dumps contained an average of only 110 ppb. Hence, much less lead would be introduced into streams if the snow were dumped on nearby land rather than directly into the water. This viewpoint is supported by the data of Hirao and Patterson (1974) who measured lead concentrations in Thompson Canyon which is located in the crest of the high Sierra in California. Lead is coprecipitated with snow in that region as very little moisture falls as rain. It was found that 98 percent of the industrial lead entering the canyon as aerosols remains there. The chelating humus fraction of the soil apparently extracts most of the lead from snow meltwaters because very little lead was found in streams leaving the canyon.

7.4.2 Mobility and Persistence in Water

In the absence of suspended solids the solubility of lead in water is dependent on pH, salt content, and partial CO_2 pressure. Equilibrium calculations show that the total solubility of lead in hard water is about 30 ppb and 500 ppb in soft water (Davies and Everhart, 1973). In soft water with a pH of 5.4 or less, $PbSO_4$ is present and limits the lead concentration in solution. Above pH 5.4, $PbCO_3$ and $Pb_2(OH)_2CO_3$ are the limiting factors in lead concentration. In hard water a pH greater than 6.0 is the level at which the above carbonates are present and cause a corresponding limitation. The most important factor in determining lead solubility in both of these waters is the carbonate concentration which in turn depends on the partial pressure of CO_2 and the pH. The equilibria involved in the solubility of lead are presented in Figures 7.12 and 7.13 for soft and hard water, respectively. The C_{Pb} lines gives the concentration of the lead in solution.

Because most natural waters have a pH greater than 7, the upper limit on the concentration of lead that occurs in lakes, rivers, or underground water is determined by the solubilities of lead carbonate and lead hydroide. This solubility limit can be low for the more alkaline and moderately mineralized waters which are commonly used for water supplies in much of the U.S. Fortunately, treatment of city water supplies usually keeps the pH high enough to maintain lead at a low concentration. Hence, lead concentrations will be below the 50 micrograms per liter standard for drinking water of the U.S. Public Health Service. However, where dissolved solids in water are low and the pH is less than 7, lead can be present in amounts greater than the above standard (Hem and Durum, 1973). When particulate matter is present, the lead content of water can be much greater than the equlibrium solubility due to adsorption of lead ions on particle surfaces. The actual thermodynamic equilibrium solubility is unchanged, however.

Because at least twice as much lead is found in atmospheric precipitation as in water supplies, Lazrus, et al., (1970) concluded that there is some process by which lead is depleted after precipitation reaches the earth's surface. Other investigators have reported lead in suspended matter to be insoluble in surface waters, and to be removed by natural sedimentation or

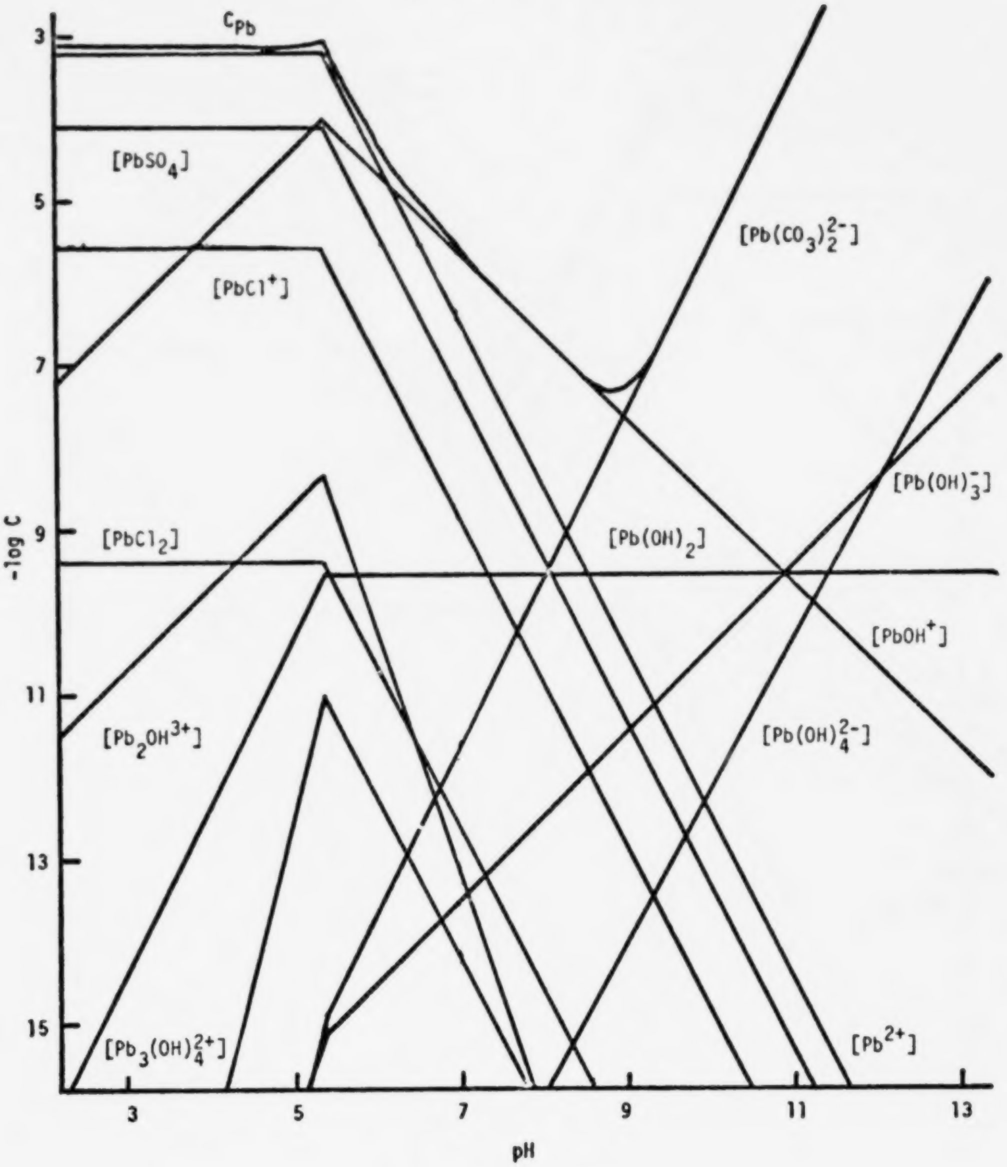


Figure 7.12 Solubility and species distribution for Pb (II) in soft water. Adapted from Davies and Everhart (1973).

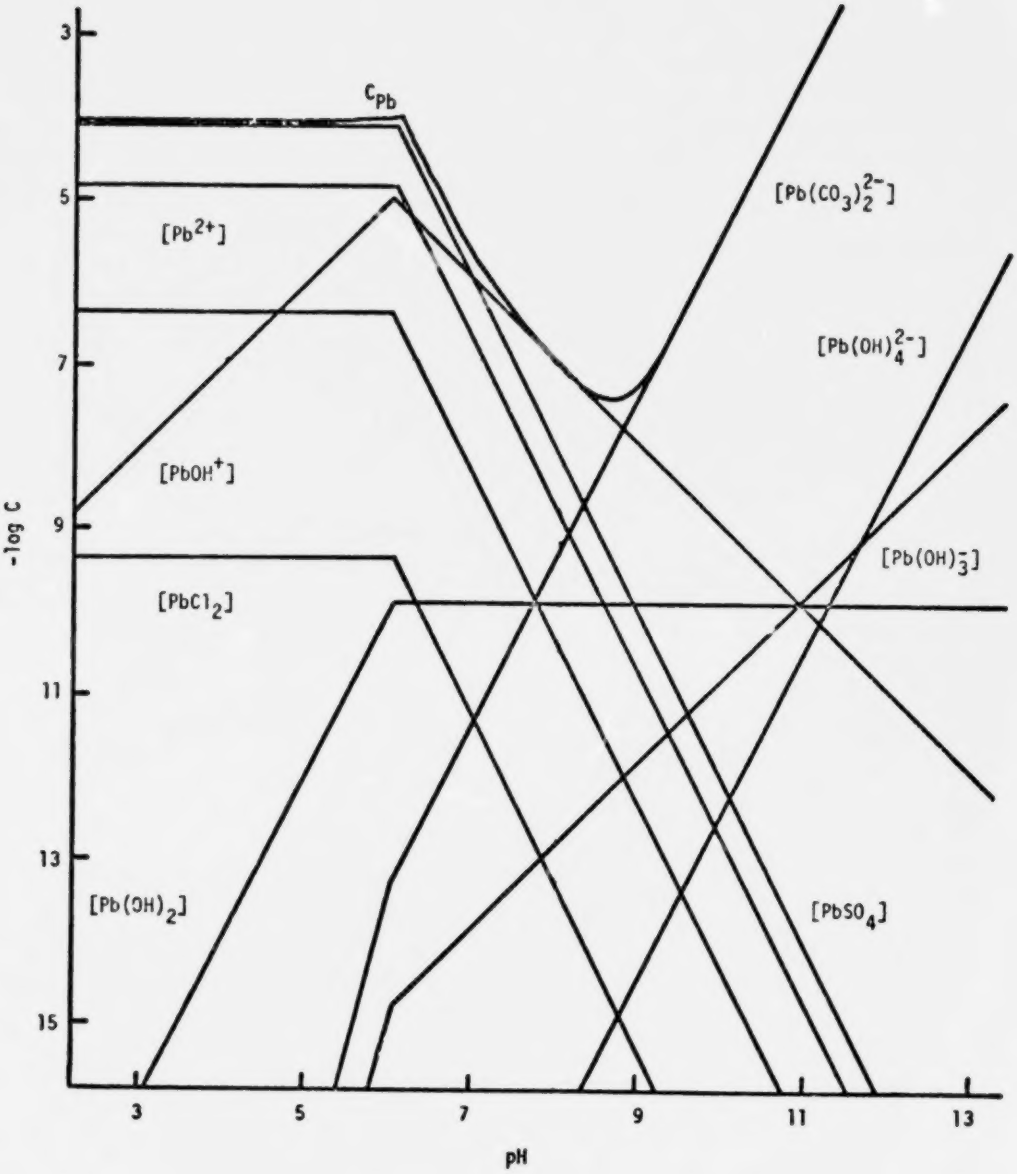


Figure 7.13 Solubility and species distribution for Pb (II) in hard water. Adapted from Davies and Everhart (1973).

filtration (National Academy of Sciences, 1972). The lead present in precipitation appears to contribute more to the pollution of sediments than to the pollution of water; therefore it is unlikely that precipitation will have a significant effect on the concentration of this element in potable waters (Harrison, et al., 1975b).

Some insight into the cycle of lead in water can be gained from the ratios of the various lead isotopes. Lead in surface ocean waters and recent precipitation is isotopically different from that found in marine sediments deposited in the geologic past. The isotope composition of lead in surface waters is typical of a mixture of lead ores from mines (Chow, 1968). Lead from man-made sources is obviously being discharged into the rivers and thence into the oceans.

It has been calculated that industrial lead is being added to the oceans at about ten times the rate of introduction by natural weathering (Chow and Patterson, 1959 and 1962). This additional lead in the oceans can be transported downward by physical processes of mixing and diffusion. However, one of the most effective agents in removing it from the surface layer is the biological process associated with sedimentation.

7.4.3 Mobility and Persistence in Soil

The nature of the lead compounds in soil that originate in automobile exhausts and that are formed near roadways was determined by Olson and Skogerboe (1975). Samples were collected from the top centimeter of surface soil or from street dust in four different parts of the U.S. Lead sulfate accounted for the major portion of the lead present in the samples. A small amount of $PbO \cdot PbSO_4$ and traces of lead oxides were found in some of the specimens, while PbS was detected in a sample from the Missouri Lead Belt. In view of the work by Ter Haar and Bayard (1971) which showed that only about 3 percent of the aerosol lead in "old" exhaust particulates was $PbSO_4$, it appears that much of the conversion to lead sulfate occurs after the lead compounds are deposited on the soil.

Lead can also be held by the humic acids in soil, either through formation of salts or by coordination. When humic acids from various soils were treated with a lead solution, the carbonyl (C=O) functionality disappeared, and the carboxylic acid (COOH) function was converted to the corresponding salt (Hildebrand and Blum, 1974). As the pH of the soil humus was decreased from 8 to 3, the amount of lead fixed was reduced from 112 to 24 millequivalents per 100 grams of humus. These results show that soil condition has an important effect on the amount of lead retained.

In general, lead deposited on the soil is retained near the surface, and its concentration drops off rapidly with depth of the soil. However, it has been observed that this retention does not always occur, and that sodium chloride is capable of leaching the lead from surface layers (Vandenbeele and Wood, 1972). Such a situation would occur where salt is used to melt snow and ice on highways.

There is some evidence that lead tends to be moved upward in the earth's crust. Swaine and Mitchell (1960) found that in Scottish soils there was approximately twice as much lead at the surface as there was at a depth of 125 centimeters. The soils analyzed were in uncultivated areas far from any industrial or vehicle contamination. Wright, et al., (1955) also reported similar results for Canadian soils from four areas. Swaine and Mitchell (1960) speculated that the decay of plant material formed some insoluble lead complex which concentrated near the surface.

If the lead is strictly of inorganic origin, it apparently can be leached from the soil at a fairly rapid rate. Roberts and Goodman (1973) examined surface soils in the vicinity of smelters at intervals after permanent shutdowns of the smelters. Soil depletion of the lead was relatively fast. At two badly contaminated sites (104 and 328 micrograms per gram of soil) the surface 5 centimeters lost lead at a rate that would get it down to background values within 2 to 5 years. A site with less lead (9.6 micrograms per gram of soil) and a dense grass cover lost lead at a much slower rate, and would take some 30 years to reach background.

Other evidence for fairly rapid removal of lead by leaching was obtained by Clark (1973) in an investigation of the leachate from landfills. Trace metals in the leachate were determined, and the lead concentration was found to be high as 500 ppb at a northern Illinois site. This value is ten times the allowable amount for U.S. Public Health standards and five times that permitted by the Illinois Pollution Control Board.

7.4.4 Wastewaters

It can be expected that the metal content of wastewaters will be greater than that of natural waters. Measurements made in Pittsburg, Pennsylvania, at the Allegheny County treatment plant for the first 6 months of 1973 showed that the incoming water contained an average of 119 ppb of lead (Davis and Jacknow, 1975). Of this amount about 75 ppb could be attributed to residential and commercial sources; the remainder was industrial. Primary treatment at the plant reduced the lead concentration to 55 ppb, and the secondary treatment, to 22. Similar measurements made at Muncie, Indiana, for 1972-73 showed a lead concentration of 920 ppb in the treatment plant influent. The amount of lead in the plant effluent was reduced to 170 ppb in 1972, but only to 270 in 1973. In this case the residential contribution to the 920 ppb was found to be only 120 ppb.

The waters of New York harbor are heavily contaminated by industrial wastes from a variety of sources. They contain from 130 to 700 ppb of lead depending on the location (Klein, et al., 1974). The highest values occurred in the lower East River, and the lowest were in Jamaica Bay and the Long Island waters.

A very extensive investigation of lead and other heavy metals in the wastewater effluents of the Hyperion Treatment Plant, Los Angeles, California, was conducted by Chen, et al., (1974). The lead concentration in the primary effluent was found to be 110 ppb with a reduction to 42 in the secondary effluent. Most of the lead was in the dissolved state with less than 20 percent retained by 0.2 micrometer filters. The secondary treatment removed less than 40 percent of the dissolved lead. The digested sludge from the plant contained 530 ppm by weight of lead.

Morel, et al., (1975) in a study of a chemical equilibrium model of Los Angeles County sewage concluded that lead should be present as the very insoluble sulfide, PbS. It also was concluded that at low dilution and moderate oxidation conditions, lead carbonate will precipitate because of the high concentration of carbonate in the sewage. The significant effect of oxidation is the dissolution of lead sulfide.

The effect of mixing wastewaters with seawater was also examined for the discharge from the Hyperion plant in Los Angeles (Rohatgi and Chen, 1975). Suspended solids in primary effluent containing 156 ppm by weight of lead released 53 percent of their lead content when equilibrated with seawater at a 5 to 1 dilution. The digested sludge particulates originally containing 875 ppm by weight of lead released 49 percent of the lead after 15 minutes (50 to 1 dilution) but after equilibration this was reduced to 38 percent. Hence, mixing with seawater is quite effective in reducing the amount of lead held on the wastewater solids. This effect may be the result of surface desorption caused by a high dilution ratio, the oxidation of sulfide, or complexing by anions in the seawater.

Wastewaters from a lead mine are potential sources of lead pollution. Proper management of wastes can keep the amount of lead discharged at a relatively low level. Stream monitoring in the New Lead Belt of Missouri has shown that lead concentrations in streams receiving mine effluents can be kept below 50 ppb. Values obtained during 1969-70 ranged from 0 to 40 ppb of lead (Jennett and Wixson, 1972). Heavy metals in mine wastes are precipitated rapidly in settling and treatment lagoons by making the mine water more basic (pH 7.5 to 8.2), thereby maintaining low levels of metals in the nearby streams.

7.4.5 Sediments

Significant concentrations of lead have been found in sediments from regions which have a high volume of automobile traffic or heavy industrialization. Measurements made on sediment cores from selected lakes in Wisconsin have shown that in populated areas the top 5 centimeters of sediments contained from 28 to 124 ppm by weight of lead. By contrast, sediments from remote lakes which never received any sewage effluent contained only from 3 to 10 ppm of lead (Iskandar and Keeney, 1974). In addition, it was noted that even at a depth of 50 centimeters in sediments from lakes in populated areas, there was more lead than in the top layer of sediment in isolated lakes.

Similar examination of two sedimentary cores from Lake Washington in Seattle, Washington, showed an increase in lead content from 30 to 400 ppm by weight during the past 80 years. The increased lead concentration paralleled the population increase of the area. The two major sources of lead during the period were believed to be a lead smelter in Tacoma, Washington, from 1890 to 1913, and automobile exhausts from the 1920's to the present (Crecelius and Piper, 1973).

Sediment samples from four lakes in Indiana were found to have lead concentrations of 7, 163, 184, and 345 ppm by weight. In the absence of characterization of the lakes, it is likely that automotive and industrial sources of lead can be associated with the high values. Data on sediments from a Gary, Indiana, borrow pit subject to such influences showed values which generally ranged from 200 to 493 ppm (Peyton and McIntosh, 1974).

Bottom sediments from the Illinois River near Peoria, Illinois, were analyzed by Mathis and Cummings (1973). The lead content proved to range from 3 to 140 ppm by weight, giving a mean value of 28 ppm. The latter value was 10,000 times greater than the mean for lead concentration in the river water (0.002 ppm). By way of comparison, the sediments of three nonindustrialized streams contained an average of 17 ppm of lead.

Core samples of sediment collected in the delta area of the Coeur d'Alene River in Idaho were mostly fine silt typical of mine tailings. For over 80 years mining and smelting wastes had been discharged into the river. The top layer of the sediments contained from 3,000 to 6,300 ppm by weight of lead. There was no significant decrease in metal content in the sediments collected at the river's mouth even at a depth of 52 centimeters. The lead content in the sedimentary layers followed the decreasing order clay, organic matter, silt, sand (Maxfield, et al., 1974).

The effect of a lead-zinc mineralized area on the heavy metal content of sediments in downstream reservoirs was investigated by Pita and Hyne (1975). Bottom sediments were collected from five reservoirs in Oklahoma, Kansas, and Missouri. In two of the reservoirs the lead concentration in sediments was less than 25 ppm, and in the other three average values of about 50 ppm were found. Soil in this region contains about 22 ppm lead, so the sediment was enriched with respect to the soil. Separation of sediment components according to specific gravity showed that lead was concentrated in the 2.0 to 2.9 fraction. This indicates that lead was included with clay minerals either as ions or as organometallic complexes.

Sediments collected in the coastal basins of Southern California receive lead at rates from two to seven times greater than those that existed before man-made sources of pollution contributed to lead levels. Values for the Santa Monica, San Pedro, and Santa Barbara Basins were 0.9, 1.7, and 2.1 micrograms per square centimeter of sea bottom per year as compared to natural rates of 0.24, 0.26, and 1.0, respectively (Chow, et al., 1973).

The possible solubilization of lead in bottom sediments by nitrilotriacetic acid has been explored by Gregor (1972). This compound was proposed as a substitute for phosphates in detergents. As little as 2 ppm of nitrilotriacetic acid was found to be capable of solubilizing some lead in the sediments, and 20 ppm of the acid increased soluble lead from 0.03 to 0.61 ppm in one case. Hence, the presence of complexing agents in water can cause lead concentrations to exceed the U.S. Public Health Service standard of 0.05 ppm.

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8.0 ENVIRONMENTAL INTERACTIONS AND THEIR CONSEQUENCES

8.1 SUMMARY

Various processes interact to redistribute lead in the environment. Organisms can take up lead from these media and, in some cases, can concentrate and accumulate lead. A variety of foods have a low, but measurable lead content. In some marine organisms elevated lead levels seem to be related to increased lead levels in the water. However, biomagnification of lead was not found in the different aquatic organisms.

In foods, the available data indicate that the edible portions of crop plants, including leaves, roots, and fruits generally have a lower lead content than the inedible portions. Also, the levels consumed in fresh fruit and vegetables are well below levels considered significant from the human health standpoint.

On the basis of a recent Market Basket Survey, the estimated daily average intake of lead by a U.S. adult is in the range of 57 to 233 micrograms. The comparable daily intake in the United Kingdom has been estimated at 200 and 20 micrograms for food and beverages, respectively. Absorption of ingested lead has been estimated to normally lie in the 8 to 10 percent range for adults and in the 40 to 50 percent range for infants and preschool-age children (see Section 6.2.1.2).

Comprehensive work has been initiated on the movement of lead within the various components of ecosystems. The transfer of lead through a simplifed estuarine food web and a laboratory model ecosystem with a terrestrial/aquatic interface has been described.

8.2 ENVIRONMENTAL CYCLING OF LEAD

In Section 7.3 the sources, distribution, and fate of lead in air, water and soil were described. In addition to background levels from geochemical sources, elevated levels of lead may result from industrial mining, refining, and processing steps and from the disposal of various municipal wastes. Figures 8.1 and 8.2 illustrate the environmental cycling of lead. Table 8.1 describes the environmental pathways for various lead compounds. Although the input of lead by the combustion of leaded fuels is considered to be the major environmental source of lead, other sources such as food, industrial wastes, paints, waste oils and storage batteries also contribute to the environmental burden. The fallout of lead-containing dust and its removal by rain or snow result in lead being deposited on soil and in water. The lead will then either be (1) retained in the soil and at least part of it become

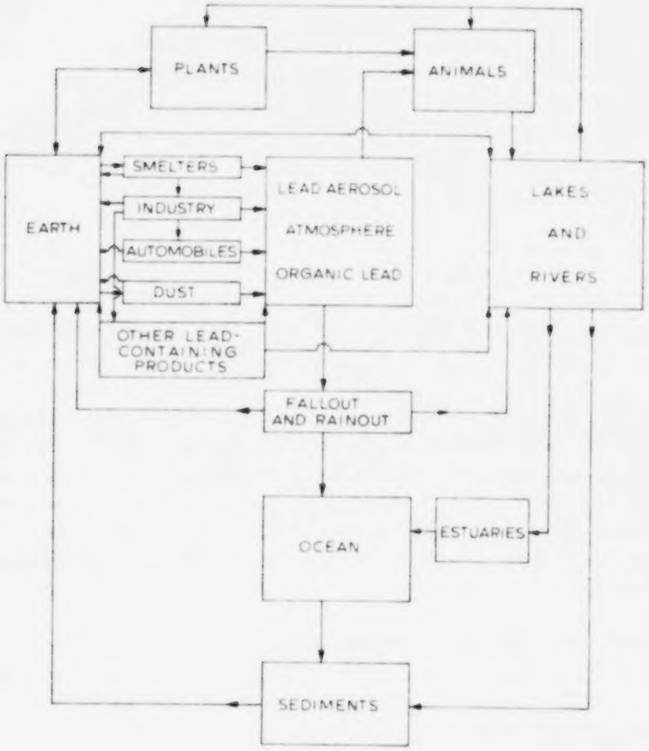
PLANTS
ANIMALS
EARTH
SMELTERS
INDUSTRY
AUTOMOBILES
DUST
OTHER LEAD-CONTAINING PRODUCTS
LEAD AEROSOL
ATMOSPHERE
ORGANIC LEAD
LAKES
AND
RIVERS
FALLOUT AND RAINOUT
OCEAN
ESTUARIES
SEDIMENTS

Figure 8.1 Ecologic flow chart for lead showing possible cycling pathways and compartments. Adapted from National Academy of Sciences, (1972).

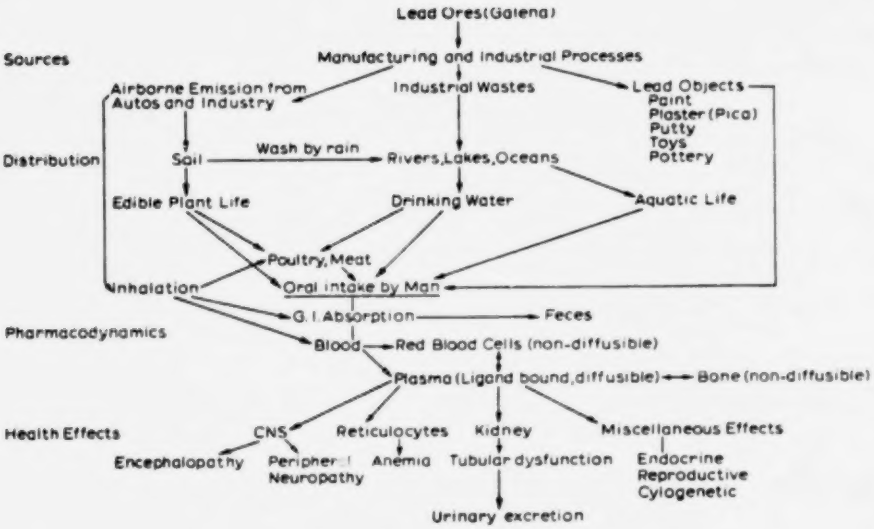
Lead Ores (Galena)
Sources
Manufacturing and Industrial Processes
Airborne Emission from Autos and Industry
Industrial Wastes
Lead Objects
Paint
Plaster (Pica)
Putty
Toys
Pottery
Distribution
Soil
Wash by rain
Rivers, Lakes, Oceans
Edible Plant Life
Drinking Water
Aquatic Life
Poultry, Meat
Inhalation
Oral intake by Man
G. I. Absorption
Feces
Pharmacodynamics
Blood
Red Blood Cells (non-diffusible)
Plasma (Ligand bound, diffusible)
Bone (non-diffusible)
Health Effects
CNS
Reticulocytes
Kidney
Miscellaneous Effects
Encephalopathy
Peripheral Neuropathy
Anemia
Tubular dysfunction
Endocrine
Reproductive
Cytogenetic
Urinary excretion

Figure 8.2 Ecodiagram of lead in the environment and its effect on man. Source: Fishbein. Reprinted with permission from The Science of the Total Environment. (c) Elsevier Scientific Publishing Company, 1974.

Table 8.1 ENVIRONMENTAL PATHWAYS FOR LEAD COMPOUNDS[a]

Chemical Compounds	Source	Transport Path	Effect	Uses
Lead acetate	Industrial processing	Air Water Land	Physiological	Dyeing and printing cottons Manufacture of lead salts Astringent (veterinary) Paint drier Lead coating of metals
Lead alloys	Industrial processing Power generation Transportation	Air Water Land Fisheries	Physiological	Slush coatings Type metals for printing Batteries Battery grids Bearing metals Solders Fusible alloys Communication cables Pipe and sheet in chemical installations Corrosion protection coatings
Lead antimonate	Industrial processing	Air Water Land		Pigment Staining glass Crockery and procelain
Lead arsenate	Industrial processing Agriculture	Air Water Land Food Consumer products	Physiological	Insecticides Veterinary medicine
Lead arsenite	Industrial processing Agriculture	Air Water Land Food Consumer products	Physiological	--
Lead azide	Industrial processing	Air Water Land	Physiological	Primer in explosives
Lead borate	Industrial processing	Air Water Land	Physiological	Paint drier and production of conductive coatings Glass Pottery Porcelain Chinaware
Lead carbonate	Industrial processing	Air Water Land	Physiological	Paints Ceramics Glazes Processing of parchment

Table 8.1 ENVIRONMENTAL PATHWAYS FOR LEAD COMPOUNDS[a] (cont'd)

Chemical Compounds	Source	Transport Path	Effect	Uses
Lead chloride	Industrial processing	Air Water Land Direct contact	Physiological	Manufacturing of white lead dyes Solder and flux
Lead chromate	Industrial processing	Air Water Land Direct contact	Physiological	Pigment Printing of fabrics Decorating china and porcelain
Lead cyanamid	Industrial processing	Air Water Land Direct contact	Physiological	Corrosion inhibitors (Antirust paints)
Lead dioxide	Industrial processing Mining	Air Water Land Direct contact	Physiological	Electrodes Dyes Rubber substitutes Manufacture pigments Analytical purposes
Lead fluorosilicate	Industrial processing	Air Water Land Contact	Physiological	Electrolyte in electrolytic refining of lead
Lead fumarate	Industrial processing	Air Water Land Direct contact	Physiological	Plastisols Phonograph records Electrical insulation
Lead iodide	Industrial processing	Air Water Land Direct contact	Physiological	Bronzing, printing Photography
Lead linoleate	Industrial processing	Air Water Land Direct contact	Physiological	Driers in paints
Lead molybdate	Industrial processing Mining	Air Water Land	Physiological	Paint Pigment
Lead monoxide, litharge	Industrial processing	Air Water Land Consumer service Contact	Physiological	Ointments Plasters Glaze Flux Pigments Analytical Driers

Table 8.1 ENVIRONMENTAL PATHWAYS FOR LEAD COMPOUNDS[a]
(cont'd)

Chemical Compounds	Sources	Transport Path	Effect	Uses
Lead naphthenate	Industrial processing	Air Water Land Direct contact Home environment Work environment	Physiological	Driers in paint
Lead nitrate	Industrial processing	Air Water Land Contact	Physiological	Match industry Pyrotechnics Chemical intermediates
Lead oleate	Industrial processing	Air Water Land Direct contact Home environment Work environment	Physiological	Driers in paint
Lead orthophosphate	Industrial processing	Air Water Land Home environment Work environment Neighborhood environment School environment Consumer products Food Waste	Physiological	Stabilizer for plastics Pigments Anticorrosive agents
Lead phosphate	Industrial processing	Air Water Land Home environment Work environment Neighborhood environment School environment Consumer products Food Waste	Physiological	Stabilizer for plastics
Lead selenide	Industrial processing Mining	Air Water Lead Environment	Physiological	Semiconductor Infrared detector
Lead silicate	Industrial processing	Air Water Land Environment	Physiological	Glass ceramics
Lead stannate	Industrial processing	Air Water Land Environmental contact	Physiological	Ceramics

Table 8.1 ENVIRONMENTAL PATHWAYS FOR LEAD COMPOUNDS[a]
(cont'd)

Chemical Compounds	Sources	Transport Path	Effect	Uses
Lead subacetate	Industrial processing	Air Water Land Food	Physiological	Sugar analysis
Lead sulfate	Industrial processing Mining	Air Water Land Contact	Physiological	Pigments Batteries Lithography Fabrics
Lead sulfide	Mining Industrial processing	Air Water Land Contact	Physiological	Photoelectric cell Infrared detector Photosensitive resistor circuits
Lead telluride	Mining Industrial processing	Air Water Land Contact	Physiological	Photoelectric cell Infrared detector Photosensitive resistor circuits
Lead tetraoxide, red lead	Industrial processing	Air Water Land	Physiological	High voltage lightning arrested Dyes Chemicals Matches Pyrotechnics Curing agents (rubber substitute)
Lead tetraethyl	Industrial processing Power generation	Air Water Land Direct contact Food	Physiological	Antiknock Fungicide
Lead tetramethyl	Industrial processing Power generation Transportation Agriculture	Air Water Land Direct contact Food	Physiological	Antiknock Fungicide Filling of Geiger counters
Trialkyl or alkyl aryl lead	Industrial processing	Air Water Land Direct contact Food	Physiological	Polymerization Catalysts Stabilizers for PVCl Electroplating Lubricating oils Biocidal agents
Lead thiocyanate	Industrial processing	Air Water Land Contact	Physiological	Primer in explosives Matches Dyes
Lead thiosulfate	Industrial processing	Air Water Land Contact	Physiological	Rubber accelerator Lead mirrors

Table 8.1 ENVIRONMENTAL PATHWAYS FOR LEAD COMPOUNDS[a]
(cont'd)

Chemical Compounds	Source	Transport Path	Effect	Uses
Lead titanate	Mining Industrial processing	Air Water Land Contact	Physiological	Pigment Ceramics
Lead tungstate	Mining Industrial processing	Air Water Land	Physiological	Pigment
Lead vanadate	Industrial processing	Air Water Land Contact	Physiological	Pigment
Lead zirconate	Industrial processing	Air Water Land	Physiological	Pigment

[a] Adapted from Lutz et al. (1970).

available for plant and animal uptake, or (2) some will be leached into groundwater. Besides wastewater discharges, lead can be removed from land masses by runoff to surface waters. The lead in these waters will appear in sediments and be ready to reenter the environmental cycle, except that ocean sediments constitute, in part, an ultimate sink for waterborne lead.

8.3 FOOD CHAINS

8.3.1 Lead in Foods

Lead enters plants and animals which are consumed as human food from the following sources:

1. Air--Dustfall and airborne particles that contain lead may settle on soil or on leaves and stems of plants.

2. Soil--Lead is present in all soils. The content is increased by lead from dustfall or rainfall.

3. Water--Lead is widely distributed in natural waters, both fresh and marine. Rainfall also contains lead derived from atmospheric particles.

The lead content of food or forage plants is related to the amount that is applied topically to exposed areas of edible leaves, stems, and fruit by rainfall or dustfall, and to the amount that is translocated from soil and surface and/or ground waters through the roots to stems, leaves, and fruit (Bethea and Bethea, 1975; Ewing and Pearson, 1973; Kehoe et al., 1968; Haley, 1969; Lagerwerff, 1970; Leland et al., 1975; Ter Haar, 1970; see Sections 4.1 and 4.3.3). Lead may accumulate differentially in different portions of plants, in varying quantities depending upon weather, proximity to highways, traffic patterns, etc. (Brandt, 1970; Dedolph et al., 1970; Harley, 1970; Leland et al., 1975; Motto et al., 1970; Schuck, 1970; Schuck and Locke, 1970). The lead content of portions that are eaten by human or livestock are most important from the health standpoint (Haley, 1969; International Lead Zinc Research Organization, 1972 a,b; Kolbye et al., 1974; Lagerwerff, 1970; Ter Haar, 1970).

For meats, milk, eggs and other products from domestic livestock, the lead content is related to that of the feed, forage and water consumed by the animals (Engel et al., 1971; Ewing and Pearson, 1973; Guss, 1970; Lynch et al., 1974). In the case of fish and shellfish, the lead content is related to that of the aquatic (fresh, brackish or marine) environment and to the uptake of lead by organisms such as plankton in the food chain (Dorn et al., 1972; Leland et al., 1975; Loutit et al., 1973).

In addition to the lead derived from air, soil, and water, foods may contain lead derived from glazed vessels and metal containers sealed with lead solder (Clark, 1972; Harris and Elsea, 1967; Klein and Namer, 1970; Mitchell and Aldous, 1974). Lead poisoning has occurred from the consumption of homemade apple cider made in lead-lined earthenware vessels and illegal alcohol or "moonshine" produced in old automobile radiators in the Southeastern states (Palmisano et al., 1969; Walls, 1969). Lead has been eliminated from food processing equipment, but old cooking utensils lined with lead alloys evidently still exist, at least in the United Kingdom (Egan, 1972).

8.3.1.1. Food and Forage Plants--

A substantial body of published data exists on the lead content of food and forage crops, including cereals, vegetables and fruits. Tables 8.2 and 8.3 summarize typical values for the lead content of cereals and vegetables, and of fruits, respectively.

The available data on portions of crop plants whose lead content is derived from both air and soil indicate that soil uptake is the more important source. Lead from the air generally deposits on the leaves and outer portions of edible plants such as husks, as well as on the soil. It appears that uptake of lead through the stomata of leaves may be considerably less than that taken up from soil through the roots (Dedolph et al., 1970; Ter Haar, 1970). However, crops grown close to highways (within 30.4 meters or 100 feet) having a heavy traffic volume may have high levels of lead contamination on the leaves and outer portions (Lacasse, 1970; Motto et al., 1970; Ter Haar, 1970). The question of whether or not lead is translocated from the leaves or roots to other portions of crops has not been resolved (Dedolph et al., 1970; Lacasse, 1970; Lagerwerff, 1970; see Section 4.3.3). The available data indicate that the edible portions of crop plants including leaves, roots and fruits generally have a lower lead content than inedible portions. Data obtained by the Food and Drug Administration from analyses of "market basket" samples of food purchased in retail establishments indicate that levels of lead consumed in fresh fruits and vegetables are well below levels considered significant from the human health standpoint (Kolbye et al., 1974).

Leafy wastes from food crops that contain high levels of lead may be a hazard to domestic livestock if used as a component of feed. For example, note in Table 8.2 the considerably higher lead content of corn stalks, leaves, and husks as compared to the kernels, and of unharvested cabbage leaves as compared to the head. The type of lead poisoning in cattle and horses is more fully discussed in Section 5.5.2.

Possible hazards from lead contamination of homegrown vegetables has only recently been considered. A warning, for example, was recently issued by the Idaho Department of Health and Welfare to residents within a 6.4-km (4-mile) radius of a lead smelter that homegrown vegetables may have high levels of lead (Anon, 1975). It is likely, however, that vegetable contamination in smelter areas is primarily a problem of deposition of lead particularly on the external portions of the plants rather than high concentrations of lead in the plant tissues themselves. Thus, thorough washing should remove most of the lead deposited on the surface. In any event, unless the garden provides a substantial proportion of the total diet, the effects of lead contribution

TABLE 8.2 LEAD CONTENT OF CEREALS AND VEGETABLES

Products	Lead Content, ppm	Sample State	Reference
Wheat, heads	1.0-2.0	Dry	Warren and Delavault (1962)
grain	0.16-0.18	Dry	Ter Haar (1970)
Oats, heads	0.3-2.0	Dry	Warren and Delavault (1962)
Corn, tassels	19-1742	Dry	Motto et al.,(1970)
leaves	30-329	Dry	Motto et al.,(1970)
stalks	3.1-13	Dry	Motto et al.,(1970)
kernels	0-2.6	Dry	Motto et al.,(1970)
cobs	0.9-5.6	Dry	Motto et al.,(1970)
Barley, heads	0.5-2.0	Dry	Warren and Delavault (1962)
Rye, heads	0.3-7.0	Dry	Warren and Delavault (1962)
grass	2.4-14.2	Dry	Dedolph et al.,(1970)
Cabbage, heads	1.0-1.1	Dry	Ter Haar (1970)
	< 0.01-0.51	Wet	Thomas et al.,(1972)
unharvested leaves	4.5-5.8	Dry	Ter Haar (1970)
Cauliflower, hearts	0.9	Dry	Warren and Delavault (1962)
leaves	2.0	Dry	Warren and Delavault (1962)
Broccoli, flowers	0.19-0.30	Wet	ILZRO (1972a)
stalks	0.04	Wet	ILZRO (1972a)
Brussel sprouts	< 0.01-0.24	Wet	Thomas et al.,(1972)
Collards	0.25-0.50	Wet	ILZRO (1972a)
Celery	< 0.01-0.02	Wet	ILZRO (1972a)
	0.01-0.02	Wet	Thomas et al.,(1972)
Spinach	0.10-0.25	Wet	ILZRO (1972a)
Watercress	0.01-0.33	Wet	Thomas et al.,(1972)
Lettuce, leaves	8.7-159	Dry	Motto et al.,(1970)
	3.2-6.6	Dry	Ter Haar (1970)
	1.0-9.0	Dry	Warren and Delavault (1962)
roots	20-150	Dry	Motto et al.,(1970)
Lettuce, Romaine, outer leaves	0.10-0.18	Dry	ILZRO (1972a)
inner leaves	< 0.01-0.01	Wet	ILZRO (1972a)
Artichokes, outer leaves	0.04	Wet	ILZRO (1972a)
inner leaves	< 0.01	Wet	ILZRO (1972a)
Potatoes, leaves	20-530	Dry	Motto et al.,(1970)
stems	14-53	Dry	Motto et al.,(1970)
roots	7.6-100	Dry	Motto et al.,(1970)
tubers	1.2-14	Dry	Motto et al.,(1970)
	0.30-0.33	Dry	Ter Haar (1970)
	< 0.01-0.14	Wet	Thomas et al.,(1972)

TABLE 8.2 LEAD CONTENT OF CEREALS AND VEGETABLES
(Continued)

Products	Lead Content (ppm)	Sample State	Reference
Potatoes, tubers, peel	7.4-10.4	Dry	Motto et al., (1970)
tubers, inner portion	0.02	Wet	ILZRO (1977a)
	3.3-4.1	Dry	Motto et al., (1970)
Onions	<0.01-0.38	Wet	Thomas et al., (1972)
Beets, roots	1.6-6.0	Unspecified	de Treville (1964)
	1.0-6.0	Dry	Warren and Delavault (1962)
tops	2.0-10.0	Dry	Warren and Delavault (1962)
Carrots, tops	25-218	Dry	Motto et al., (1970)
	4.0-7.0	Dry	Warren and Delavault (1962)
leaves	83-152	Dry	Motto et al., (1970)
stems	16-23	Dry	Motto et al., (1970)
roots	0.05-0.06	Wet	ILZRO (1972a)
	3.3-24	Dry	Motto et al., (1970)
	1.7-2.1	Dry	Ter Haar (1970)
		Wet	Thomas et al., (1972)
	2.0	Dry	Warren and Delavault (1962)
inner portion	<0.01	Wet	ILZRO (1972a)
Leeks	0.04-0.07	Wet	Thomas et al., (1972)
Radish, leaves	2.3-16.4	Dry	Dedolph et al., (1970)
roots	0.8-2.0	Dry	Dedolph et al., (1970)
	0-0.2	Unspecified	de Treville (1964)
Peas, pods and peas	<0.01-0.02	Wet	ILZRO (1972a)
pods	<0.01-0.02	Wet	ILZRO (1972a)
peas	0.03	Unspecified	de Treville (1964)
Beans	0.15-0.26	Unspecified	de Treville (1964)
	1.2-1.4	Dry	Ter Haar (1970)
Beans, leaves	7.9-20.9	Dry	Ter Haar (1970)
Cucumbers	0.01-0.03	Wet	Thomas et al., (1972)
Tomatoes, leaves	37-276	Dry	Motto et al., (1970)
blades	31-87	Dry	Motto et al., (1970)
petioles	8-16	Dry	Motto et al., (1970)
stems	3.9-166	Dry	Motto et al., (1970)
fruit	0.59-0.72	Dry	Ter Haar, 1970
	0.01-0.14	Wet	Thomas et al., (1972)
peels	3.6-16	Dry	Motto et al., (1970)
pulp	3.1-6.8	Dry	Motto et al., (1970)
Rhubarb, stems	2.0-4.0	Dry	Warren and Delavault (1962)
leaves	8.0-11.0	Dry	Warren and Delavault (1962)
Mushrooms	0.03-0.04	Wet	Thomas et al., (1972)

TABLE 8.3 LEAD CONTENT OF FRUITS

Products	Lead Content, ppm	Sample State	References
Apples, whole fruit	0.12-0.3	Unspecified	de Treville (1964)
	$<$0.01-0.37	Wet	Thomas et al., (1972)
skin	$<$0.01-0.24	Wet	Thomas et al., (1972)
flesh	$<$0.01-0.05	Wet	Thomas et al., (1972)
Pears, whole fruit	0.18	Unspecified	de Treville (1964)
	0.02-0.04	Wet	Thomas et al., (1972)
skin	$<$0.01-0.23	Wet	Thomas et al., (1972)
flesh	$<$0.01-0.03	Wet	Thomas et al., (1972)
Peaches	0.04-0.08	Unspecified	de Treville (1964)
Cherries	0.12	Unspecified	de Treville (1964)
Plums	0.06-0.16	Wet	Thomas et al., (1973)

from contaminated produce should be diluted in the total pool of food consumed so that this source probably would contribute very little total lead in a well balanced diet.

8.3.1.2. Processed Fruit and Vegetable Products--

Table 8.4 summarizes reports of analyses of lead contamination in canned, frozen, and dehydrated fruit and vegetable products. The lead content of frozen beans, peas and carrots was below the detectable limit of the analytical method used. Interestingly, these products together with frozen spinach and frozen potatoes had a lower lead content than that of the corresponding fresh products given in Table 8.2. The canned fruit products listed in Table 8.4 had significantly higher lead contents (99.9 percent confidence level) than the corresponding fresh products listed in Table 8.3.

It is believed that these differences between fresh and canned products result from the release of lead from solder used along the seam of the can. Fruits and vegetables that are processed are washed thoroughly. This treatment removes a portion of the lead on the surface of leaves, roots, or fruit as indicated in data published by International Lead Zinc Research Organization (1972a).

Analyses of the lead content of canned tomato paste by Mitchell and Aldous (1974) revealed that higher lead levels (up to 500 micrograms per liter) were obtained in samples taken near the soldered seam than in samples taken in the center or opposite side of the can. Since the pH of tomato paste is approximately 4.0, they concluded that lead was leached from the soldered seam. This effect was particularly evident after the open cans were held at room temperature for 24 hours. Products in cans having a high seam length to volume ratio (>1.25 and 0.75 to 1.25) had a higher lead content than those in cans having a lower ratio (<0.75). The high ratio cans included mainly baby food and other small juice cans.

A survey conducted by the National Canners Association (1977) examined lead content of various common vegetables, fruits, and juices prior to canning and after storage in the can for 1-1/2, 3, 6, and 12 months. The NCA data (Table 8.5) offers strong support that: (1) food can absorb substantial quantities of lead from cans, and (2) lead concentration in canned food increases with the length of storage. Several foods such as grapefruit juice, orange drink, corn, and tomatoes approximately doubled their initial lead content after 1 year in storage.

8.3.1.3. Milk and Infant Formulas--

There is considerable concern about the lead content of milk and processed milk products since these foods comprise a substantial proportion of the diet of infants and children. Various data, past and present, exist with respect to lead levels in milk, processed milk products, infant formulas and human milk. These data are assembled by product in chronological order in Table 8.6.

TABLE 8.4 LEAD CONTENT OF PROCESSED FRUITS AND VEGETABLE PRODUCTS

Products	Lead Content, ppm	Sample State	References
Beans, frozen	< 0.01	Wet	ILZRO (1972a)
Beans, baked	0.19-0.67	Wet	Thomas et al.,(1973)
Carrots, frozen	< 0.01	Wet	ILZRO (1972a)
Corn, canned	0.00-3.00	Wet	National Canners Association (1977)
Peas, frozen	< 0.01	Wet	ILZRO (1972a)
Peas, canned	0.00-1.46	Wet	National Canners Association (1977)
Spinach, canned	0.13-0.95	Wet	Thomas et al.,(1973)
Spinach, frozen	0.07	Wet	ILZRO (1972a)
Potatoes, frozen	0.01	Wet	ILZRO (1972a)
Tomatoes, canned	0.32-0.63	Wet	Thomas et al.,(1973)
Apples, canned	0.12-1.14	Wet	Thomas et al.,(1973)
Apricots, canned	0.52-1.48	Wet	Thomas et al.,(1973)
Apricots, dried	0.24	Unspecified	de Treville (1964)
Black currants, canned	0.17-3.90	Wet	Thomas et al.,(1973)
Damsons, canned	0.37-0.74	Wet	Thomas et al.,(1973)
Grapefruits, canned	0.19-0.54	Wet	Thomas et al.,(1973)
Oranges, canned	0.10-0.22	Wet	Thomas et al.,(1973)
Peaches, canned	0.26-0.50	Wet	Thomas et al.,(1973)
Pineapples, canned	0.14-0.54	Wet	Thomas et al.,(1973)
Plums, canned	0.17-0.98	Wet	Thomas et al.,(1973)
Prunes, canned	0.15-0.73	Wet	Thomas et al.,(1973)
Raisins	0	Unspecified	de Treville (1964)
Rhubarb, canned	0.10-2.57	Wet	Thomas et al.,(1973)
Strawberries, frozen	0.02	Wet	ILZRO (1972a)
Fruits and vegetables, dried	1.0-2.0	Unspecified	de Treville (1964)

Table 8.5 LEAD UPTAKE IN CANNED VEGETABLES, FRUITS, AND JUICES[a]

Food Product	Lead Concentration, ppm[b]	Percent Contributed by Can
Corn		
initial	0.46	
6 months	0.59	92
1 year	0.93	95
Green beans		
initial	0.48[c]	
6 months	0.35	49
1 year	0.39	54
Peas		
initial	0.33	
6 months	0.40	80
1 year	0.37	78
Tomatoes		
initial	0.31	
6 months	0.55	89
1 year	--	--
Applesauce		
initial (mean)	0.27	
6 months	0.32	75
1 year	0.38	79
Fruit cocktail		
initial	0.22[c]	
6 months	0.21	62
1 year	--	--
Grapefruit juice		
initial	0.04	
6 months	0.09	100
1 year	0.30	100
Tomato juice		
initial	0.25	
6 months	0.28	82
1 year	--	--
Orange drink		
initial	0.05	
6 months	0.11	91
1 year	0.11	91

[a] Source: National Canners Association, (1977).

[b] Values are means of approximately 12-50 samples.

[c] Anomalous mean, caused by distribution extremely skewed to the right.

Table 8.6 LEAD CONTENT OF MILK AND INFANT FORMULAS

Milk Product	Year of Sampling	Mean, ppm	Range	Method[d]	Reference
Canned evaporated milk					
skimmed	1971	1.04	0.30-2.30	AAS[d]	Lamm et al., 1973
	1972-73	0.06	0.04-0.07	AAS	Lamm and Rosen, 1974
regular	1968	0.81[c]		AAS	Murthy and Rhea, 1971
	1971	0.36	0.30-0.40		Lamm et al., 1973
	1972-73	0.11	0.04-0.22	NAAS	Lamm and Rosen, 1974
	1972-74	0.14	0.03-0.91	undetermined	Ministry of Agriculture, Fisheries and Food, 1975
	1973	0.202	0.01-0.820	AAS	Mitchell and Aldous, 1974
	1973-74	0.125	0.02-0.37		U.S. DHEW (FDA), 1975
		0.12	0.01-0.46		Schmidt, 1974
Infant Formula					
Concentrate	1972-73	0.083	0.04-0.12	NAAS	Lamm and Rosen, 1974
		0.09			National Canners Association, 1973 (unpublished) cited in Kolbye et al
		0.09	0.06-0.13	AAS	Kolbye et al. 1974
Ready to serve (diluted)					
Modified Milk I	1968	0.170		AAS	Murthy and Rhea, 1971
Modified Milk II	1968	0.210		AAS	Murthy and Rhea, 1971
Lamb Meat Base	1968	0.256		AAS	Murthy and Rhea, 1971
Soya Base	1968	0.272		AAS	Murthy and Rhea, 1971
	1972-73	0.033[b]	0. -0.08	NAAS	Lamm and Rosen, 1974
	1972-74	0.05		undetermined	Ministry of Agriculture, Fisheries and Food, (London) 1975
Homogenized Milk (cow)	1971	0.04		AAS	Lamm et al., 1973
	1972-73	0.005[a]		NAAS	Lamm and Rosen, 1974
	1973	0.04		AAS	Mitchel and Aldous, 1974
	1972-74	0.02	0.02-0.07	not stated	Ministry of Agriculture, Fisheries and Food, 1975
		0.005		dithizone	Brandt and Bentz, 1971
		0.042[e]	0.009-0.1540	AAS	Pinkerton et al., 1973
		0.042		photon activation	Dutilh and Das, 1971
		0.049	0.023-0.079		
Human breast milk					
	1971	0.02	0. -0.065	AAS	Lamm et al., 1973
	1972-73	0.005		NAAS	Lamm and Rosen, 1974
		0.010[e]	0.006-0.202	AAS	Murthy and Rhea, 1971
		0.012		AAS	Murthy and Rhea, 1971

[a] Detection limit 0.005 ppm.

[b] Seamed cans and bottles averaged.

[c] Average of four brands.

[d] AAS = flame atomic absorption spectrophotometry; NAAS = nonflame AAS.

[e] Median, rather than mean.

Numerous articles in recent years have discussed the difficulty of accurately quantifying lead in milk in the parts per billion range (Lamm and Rosen, 1974; Brandt and Bentz, 1971; Kolbye et al., 1974 and Dutilh and Das, 1971). Differences as large as tenfold between different investigators and/or analytical techniques in analysis of the same product are not uncommon. Cooperative studies involving several laboratories using standardized methods of sample preparation and analytic techniques on identical samples have revealed poor performance and extreme variability between laboratories. Accuracy worsens as the level of lead decreases, particularly as the lead level decreases below 1 ppm, which is typical of milk products. In addition, the ubiquity of lead magnifies the possibility for sample contamination. On the other hand, trace metal loss during destruction of the sample matrix also contributes to error. These problems notwithstanding, several generalizations can be made from the data shown in Table 8.6.

The lead content of human breast milk and fresh, homogenized cow's milk (market milk) are quite low in comparison to those milk products which have been canned, evaporated or mixed with additives (i.e., infant formulas.) This is as expected, for the lead concentration of the plasma is low and remarkably constant over a wide range of red blood cell lead levels (Lamm and Rosen, 1974), and, since only a small fraction of total plasma can be ultrafiltered through a molecular weight cut-off of approximately 2,000, one should anticipate a naturally low level of lead in milk.

Lynch, et al., (1974) also confirmed that very little lead is excreted via the milk, even after administration of substantial amounts of lead. 11.0 milligrams of lead, as $Pb(CO_3)_2$, per kilogram of body weight was administered to Holstein cows. This lead level did not produce serious physiological changes despite a large body burden. The lead content of whole milk (5.9 ppb), was lower than the mean lead content (49 ppb) of market milk as determined in a national survey by Murthy, et al., (1967). However, the lead content of milk did not decrease to background levels until 34 days after dosing the cattle. Lead content of milk can also be influenced by the lead content of feed and grass, particularly near highways, and the licking of metal objects or painted surfaces by cows.

Pinkerton, et al., (1973) collected human milk from mothers in a breast-feeding club in Cincinnati, Ohio, and bovine milk from individual cows on farms producing milk for the Cincinnati area (Table 8.6). Chemical analyses revealed that human breast milk contained about one-fourth the lead of bovine milk. Median milk lead values were 0.010 and 0.042 ppm, respectively, for humans and cows. Based on this study, a bottle-fed infant could theoretically take in about thirty times the lead of an exclusively breast-fed infant.

Whereas analyses of human milk and homogenized cow's milk have shown low levels of lead, past studies have indicated serious contamination problems in canned evaporated milk. Lead content of other processed milk products (e.g., infant formulas) is generally intermediate between the levels of "natural" milks and those of canned evaporated milk (Table 8.6). Data in 1968 on four brands of evaporated milk indicated concentrations of 0.8 ppm; four brands of infant formulas averaged about 0.4 ppm lead (Murthy and Rhea, 1971).

As recently as 1974, levels of 0.5 ppm were frequently found in canned milk when levels below 0.2 ppm would have been expected on the basis of concentration of whole milk (Kolbye, et al., 1974). These and other available data suggest the need for further research, particularly with regard to solder and flux operations in canning evaporated milk. Unlike other food products, evaporated milk traditionally has been packed in a can having a soft solder plug.

Murthy and Rhea (1971) reported that the ratio of tin to lead in the filling solder affected lead uptake by evaporated milk. When the ratio was 60:40 and large amounts of solder were allowed access to the milk, lead uptake of 0.34-1.60 ppm was observed whereas samples not exposed to solder had 0.05-0.37 ppm. No significant difference was seen in lead uptake by evaporated milk between a 50:50 filling solder and a 10:90 for internal seams. With solder pellets present inside, canned milk showed 0.10-0.54 ppm lead (Engst and Waggon, 1965).

The evaporated milk industry was informed of the need to reduce these levels and the industry has responded by instituting changes in canning operations and improving quality control procedures. A general declining trend from levels as high as 0.5 ppm to 0.1 ppm over the past 5 - 7 years is evident from Table 8.6.

The data obtained by Lamm and Rosen (1974) showed a decrease in lead content of evaporated milk and infant formulas in a 1972-73 survey as compared to that determined in a 1971-72 (Lamm, et al., 1973) survey. These results have quite reasonably been questioned on the basis of a change from flame to nonflame atomic absorption spectrometric analyses (Holliday, et al., 1974; Sarett, 1974). As shown in Table 8.6, Lamm and Rosen's (1974) data shows significantly lower levels for all milk products (including market milk and human milk) than Lamm, et al.'s (1973) study. Thus, much of the discrepancy between the two studies is probably attributable to analytical techniques, rather than an actual decrease of the magnitude suggested (ca 10X).

Mitchell and Aldous (1974) obtained higher lead levels in canned evaporated milk (mean, 0.20 ppm; range, 0.01 to 0.28 ppm) using flame atomic absorption spectrometry than did Lamm and Rosen (1974) using a nonflame method (mean, 0.10 ppm; range, 0.04 to 0.22 ppm).

More recent Food and Drug Administration (FDA) analyses indicated that the mean lead content of 80 canned, evaporated milk samples was 0.125 ppm, with a range of 0.02 to 0.37 ppm (Kolbye, et al., 1974). The results of an industrial survey of 3000 canned, evaporated milk samples using a FDA-approved method showed a mean value of 0.12 ppm Pb, with the highest level in the range of 0.01 to 0.46 (U.S. DHEW, 1974).

The food industry has been moving toward elimination of the plug-type metal container. This should aid in minimizing the levels of lead in evaporated milk and related products.

In addition, the importance of evaporated milk in infants nutrition has been in a long-term declining trend over the past 20 years. As reported by Fomon (1974), whereas in 1958 the feeding of about 42 percent of infants through 2 months of age was based on evaporated milk formulas, this had decreased to about 2 percent by 1972.

Evaporated milk has largely been replaced by formulas based on soybeans, more nutritionally complete and more easily digested by infants than cow's milk. Evidence in support of this comes from the results of two surveys conducted by one of the major formula producers (Martinez, personal communication, 1977), which indicated the following proportions of infants using evaporated milk formulas:

	Evaporated Milk, percent	
	1976	1971
Hospital period	0.1	0.8
to 2 months	1.0	4.2
3-4 months	2.2	4.0
5-6 months	2.2	3.5

These infant formulas are available either concentrated, requiring dilution before use, or ready-to-use. Both types are packed in regular side-seamed cans, and do not use the plug-type evaporated milk style can.

The use of canned milk (condensed and evaporated) has in general also been in a long-term declining trend in the United States, as indicated by U.S. Department of Agriculture 1977 Statistics.

Year	Millions of lb
1967	1,572
1968	1,497
1969	1,376
1970	1,214
1971	1,186
1972	1,102
1973	1,057
1974	1,000
1975	924
1976	862
1977	788

Commercial infant formulas are packed in the usual rigid seamed cans and available information does not indicate a present hazard from lead contamination in these formulas.

Analyses of infant formulas packed in 8-ounce and 30-ounce seamed cans and in 4-ounce glass nursettes did not reveal any significant differences in the lead content of the product in either of these types of containers (Lamm and Rosen, 1974). This finding has not been replicated in other studies, however. Lamm and Rosen's (1974) survey as well as a National Canner's Association survey showed averages of 0.08 and 0.09 ppm, respectively. Similarly, FDA spot analyses showed an average of 0.09 ppm in four major brands of infant formula concentrates. Diluted for use, the lead values would be reduced by 50 percent, making them comparable to market milk.

8.3.1.4 Meat, Fish and Poultry Products--

Table 8.7 presents a summary of the lead content of meat, fish and poultry products. The lead content of organ meats such as heart, kidney and liver of swine and turkeys (not shown) is usually higher than that of muscle (Dalton and Malanoski, 1969). However, the lead content of beef liver appears to be quite low compared to that of beef muscle.

The lead content for cured and smoked meat products given in Table 8.7 was reported by Kirkpatrick and Coffin (1973) on a fresh-weight basis. When these are corrected to a dry-weight basis, the highest lead level of bacon, ham, and picnic shoulders will be lower than that for pork muscle reported by Dalton and Malanoski (1969). According to Hankin, et al., (1975b), seven market samples of fresh beef and pork liver that were analyzed by the atomic absorption spectrometric method of Dalton and Malanoski (1969) contained 1.4 to 1.6 ppm Pb. Liverwurst sampled sporadically contained from 0 to 7.6 ppm Pb apparently depending upon the lead content of the ingredients used.

8.3.1.5 Beverages, Bakery Products, Sugar and Condiments--

Tables 8.8 to 8.10 present summaries of the lead content of beverages, bakery products, sugar, condiments and miscellaneous foods.

It does not appear that any of these products except fruit juices, both adult and infant types, contain sufficient quantities of lead to be of concern from the standpoint of a total dietary intake. These products have a pH in the range of 2.7 to 3.9. Mitchell and Aldous (1974) reported that the mean lead level of canned, infant products was 202 micrograms per liter as compared to 35 micrograms per liter in bottled products. They explain the higher levels in cans on the basis of the acidity of these products combined with leaching of lead from the seams in cans possessing a high seam to volume ratio.

8.3.1.6 Lead in the Human Diet--

No evidence exists at the present time of any effect of lead as a beneficial trace element in human nutrition. Various estimates have been made of the total human exposure to lead from food sources. In the United Kingdom, Tolan and Elton (1973) analyzed food samples that were representative of the average diet, and estimated that the adult daily intake of lead from food and beverages was 200 and 20 micrograms, respectively. According to Meranger and Smith (1972), lead was not present in sufficient levels in Canadian diets to cause concern. A FDA estimate based on historical data of U.S. adult intake of 337 micrograms of lead per day has been superseded by a 1972 Market Basket Survey estimate range of 57.4 to 233 micrograms per day. The latter estimate was based on actual analyses and varying assumptions concerning the actual lead content of samples having trace levels (Kolbye, et al., 1974). These authors point out the limitations in the various analytical methods for detecting lead in foods at levels below 1 ppm.

Kolbye, et al., (1974) cite a dietary survey of 333 infants in the United States, aged 1 to 12 months, in which the estimated dietary lead intake was

Table 8.7 LEAD CONTENT OF MEAT, FISH, AND POULTRY PRODUCTS

Products	Lead Content, ppm	References
Beef, roast chuck	0.71[b]	U.S. DHEW (1975)
bone of leg	3.60	Kehoe (1976)
hamburger	0.248[b]	U.S. DHEW (1975)
liver	0.089[b]	U.S. DHEW (1975)
Pork, fresh, muscle	0.54-1.33	Dalton and Malanoski (1969)
Meat, canned, cured[a]	0.01-0.30	Kirkpatrick and Coffin (1973)
Wiener (smoked or unsmoked	0.04-0.16	Kirkpatrick and Coffin (1973)
bologna	0.01-0.26	Kirkpatrick and Coffin (1973)
meat loaves	0.01-0.26	Kirkpatrick and Coffin (1973)
salami	0.01-0.30	Kirkpatrick and Coffin (1973)
pastrami and other	0.01-0.42	Kirkpatrick and Coffin (1973)
liverwurst	1.80-7.60	Hankin et al., (1975b)
bacon	0.01-0.16	Kirkpatrick and Coffin (1973)
ham	0.01-0.16	Kirkpatrick and Coffin (1973)
picnic shoulders	0.01-0.12	Kirkpatrick and Coffin (1973)
corned beef products	0.01-0.28	Kirkpatrick and Coffin (1973)
Fish, fresh		
cod, fresh, Icelandic	0.32	Zook et al., (1976)
clams, hard, Atlantic	0.28	Zook et al., (1976)
crab, body meat, Pacific	0.45	Zook et al., (1976)
lobster, Atlantic	0.55	Zook et al., (1976)
shrimp, Alaskan	0.50	Zook et al., (1976)
Fish, canned		
tuna, initial	0.34	National Canners Association (1977)
canned, 6 months after packing	0.44	National Canners Association (1977)
sardines, Dutch	0.72	Reith et al., (1974)
Poultry		
chicken, fryer	0.127[b]	U.S. DHEW (1975)
turkey, fresh, muscle	2.93-3.35	Dalton and Malanoski (1969)
Eggs, chicken	0.174[b]	U.S. DHEW (1975)
Meat, fish, and poultry (composite)	0.015	Kolbye et al., (1974)

[a] Data on canned, cured meats are expressed on a wet-weight basis.
[b] Mean.

TABLE 8.8 LEAD CONTENT OF BEVERAGES

Products	Lead Content, ppm	References
Drinking water (U.S.)	0.015[a]	U.S. EPA (1975)
Lemonade	0.004	de Treville (1964)
Soda	0.004	de Treville (1964)
Soft drinks (Holland)	0.02	Reith et al.,(1974)
Carbonated beverages	<0.008	Meranger (1970)
Tea	0.20-0.74	Ministry of Agriculture, Fisheries, and Food (1975); Reith et al.,(1974)
ALCOHOLIC BEVERAGES		
Beer (Cincinnati)	0.01-0.29	de Treville (1964)
Beer (Holland)	0.03	Reith et al.,(1974)
Wine (Holland)	0.13	Reith et al.,(1974)
Brandy (India)	0.05-0.60	de Treville (1964)
Rum (India)	0.024-0.057	de Treville (1964)
Dry Gin (India	0	de Treville (1964)
Whiskey (India)	0.027	de Treville (1964)
FRUIT JUICES		
Lime juice	0.30	Meranger (1970)
Lemon juice	0.57	Meranger (1970)
Diluted fruit drinks, canned	0.251	U.S. DHEW (1975)
Orange juice, canned frozen concentrate	0.135	U.S. DHEW (1975)
Tomato juice, canned	0.338	U.S. DHEW (1975)
Orange juice, infant	0.308-0.655	U.S. DHEW (1975)
Apple juice, infant	0.207-0.907	U.S. DHEW (1975)

[a] Median value.

TABLE 8.9 LEAD CONTENT OF BREAD AND BAKED PRODUCTS[a]

Products	Lead Content ppm[b]
Bread, whole wheat	0.42
Bread, white	0.41
Rolls, hamburger	0.45
Doughnuts, cake	0.45
Biscuit mix	0.24
Flour, all purpose	0.51

[a] Source: Zook, et al. Reprinted with permission from Cereal Chemistry. (c) American Association of Cereal Chemists, 1970.

[b] Means lead content, dry weight basis.

TABLE 8.10 LEAD CONTENT OF SUGAR, SPICES, CONDIMENTS, AND MISCELLANEOUS FOODS

Products	Lead Content, ppm	References
Sugar	0.004-0.13	de Treville (1964); Haley (1969); Kolbye et al., (1974); Ministry of Agriculture, Fisheries, and Food (1975)
Corn syrup	0.21-0.49	de Treville (1964)
Pepper, black	0.22	de Treville (1964); Haley (1969)
red	0.4	de Treville (1964); Haley (1969)
Ginger	0.08	de Treville (1964); Haley (1969)
Turmeric	0.4	de Treville (1964); Haley (1969)
Mustard seed	0.4	de Treville (1964); Haley (1969)
Cloves	0.15	de Treville (1964); Haley (1969)
Cinnamon	0.03	de Treville (1964); Haley (1969)
Salt	0.2-0.45	de Treville (1964); Haley (1969)
Coffee	0.07	Reith et al.,(1974)
Cocoa beans	0.15	Reith et al.,(1974)
Baking powder	5.0-10.0	de Treville (1964); Haley (1969)
Refined soybean oil, canned	0.02-0.10	Bergner and Rudt (1968)
Oils, fats, and shortening	0.02	Kolbye et al., (1974)

93 plus or minus 36 micrograms per day. In contrast, Lanzola, et al., (1973) estimated that the daily dietary intake of lead by children in Italy from the 4th to 12th month of life increased from 172 to 289 micrograms. Definitive information from balance studies is lacking on the absorption and retention of lead from the gastrointestinal tract in infants and small children. However, preliminary studies indicate that absorption rates in small children may be 5 to 10 times that of adults.

According to Mahaffey (1974), susceptibility to lead toxicity depends upon age, season of the year (body temperature, dehydration, ultraviolet light), calcium, phosphorus, vitamin D, dietary protein, ascorbic acid, nicotinic acid, alcohol, and other heavy metals. In rat studies, the toxicity of a given concentration of lead increased significantly when dietary intakes of calcium or iron were reduced to 20 percent of the recommended level. If these findings can be generalized to children the effects of high lead intake in children having dietary deficiencies of calcium and iron might be significantly increased (see Section 6.3.2.1).

Forty-six children, aged 24 to 47 months, selected on the basis of blood levels of lead were studied by Mooty, et al., (1975) to determine any relationship between dietary intake and plumbism (lead poisoning). There were no significant differences in protein, caloric, or iron intake of children having low blood levels of lead (10 to 25 micrograms per 100 milliliters) as compared with children having high levels (greater than 50 micrograms per 100 milliliters). However, pica, defined as chronic ingestion of crayons, clay, starch, soil, pencils, matches, paper, chipped paint and plaster was more prevalent in the children showing plumbism.

8.3.2 Terrestrial Ecosystems

There are numerous reports showing that plants take up lead and generally the concentrations in plants grown in high lead soils is greater than those grown in low lead soils. The lead content differs in various parts of the plants, roots often having the highest concentration. Translocation studies (see Section 4.3.3) indicate that lead is either unavailable to the plant or is "fixed" in the roots and only small amounts are translocated to the aboveground parts of the plant.

Following uptake, lead in the plant is distributed throughout the plant and is returned to the ground either upon removal or decay of portions of the plant. Factors that determine lead availability and its uptake and distribution within plants are identified in Section 4.1. Thus, lead can be leached from soil and the litter layers where it is available for uptake by various plants, microbes and soil invertebrates. Biological breakdown of plant materials makes lead available to soil-dwelling organisms associated with many complicated food chains and the lead they consume may subsequently become available to organisms of the next trophic level. As described in Section 4.2.2.1, lichens, fungi, mosses, and liverworts have a considerable capacity for lead uptake. The lichen Parmelia physodes has been used as a bioindicator for the intensity of lead near a smelter (Holl and Hampp, 1975). Enrichment of upper soil horizons has been attributed to mosses and liverworts which concentrate elements including lead, and then by decomposition, release them into the surface soil (Antonovics, et al., 1971; Shacklette,1965a,b). Spanish moss (Tillandsia usneoides), a vascular plant, has also been used as an indicator of lead pollution. Tissues of mosses have been found to contain decreasing lead contents with increasing distances from lead industries (Lee, 1972). However, at 800 meters from the contamination source, the amount of lead in mosses was two to three times greater than in the same species collected in uncontaminated areas.

Hemphill (1974) and Hemphill, et al., (1974) found that forage plants and soils along ore-truck routes in Missouri's Lead Belt contained elevated levels of lead and other toxic metals which decreased as distance from the highway increased. Lead concentrations averaged 280 ppm dry weight on the roads' rights-of-way and 34 ppm at 91.4 meters (100 yards), 11.6 ppm at 182.8 meters (200 yards), and 6.5 ppm at 365.6 meters (400 yards) from the highway. Blueberries had a maximum of 537 ppm along the truck routes and 172 ppm at 91.4 meters (100 yards) from the routes. The deaths of several horses in 1970 was attributed to the accumulation of toxic levels of lead in forage plants along the highway. In areas of high lead emission, insects had average lead levels (ppm, oven dry weight) of 10.3, 15.5, and 25, respectively, for species that suck plant juices, chew plant parts, and prey on other insects (Price, et al., 1974). These figures indicate a biomagnification of lead from herbivore to carnivore trophic levels. In low lead emission areas insects in the same feeding categories had average lead contents of 4.7, 3.4, and 3.3 ppm. Giles, et al., (1973) found that measurable quantities of lead were being concentrated by Japanese beetles (Papillia japonica), damselflies (Agrion maculatum), and the European mantid (Mantis religiosa) which were collected in 1970 along Interstate 83, Baltimore, Maryland's major north-south freeway. Gish and Christensen (1973) found that lead, cadmium, nickel, and zinc in soils and earthworms decreased with increasing distance from the Baltimore-Washington Parkway and U.S. Highway No. 1. The mean lead concentrations for the two highways combined were 468.3 to 53.4 ppm (soils) and 269.8 to 52.7 (earthworms) at distances of 3-48 meters (10-160 feet) from the roadway, respectively. The maximum lead level accumulated by earthworms was 331.4 ppm.

In a study of cadmium, zinc, and lead distribution in East Tennessee Van Hook (1974) found mean lead concentrations in soils and earthworms were 27 and 4.7 ppm, respectively. The mean earthworm concentration factor for lead was 0.2, ranging from 0.1 in Emory soil to 0.3 in Captina soil.

Rolfe, et al., (1972) conducted a study at the University of Illinois aimed at understanding and modeling the movements and effects of heavy metals (initially lead) in the environment. A model has been constructed which stimulates the movements and projects the accumulation points of lead in a 76-square mile watershed ecosystem in Champaign County, Illinois. The model includes components of both aquatic and terrestrial ecosystems and defines the ecosystem by a network of nodes and branches. The nodes generally represent the components of the ecosystem, and the branches indicate possible transport mechanisms between nodes. The basic network of 17 nodes and 44 branches shown in Figure 8.3 has been expanded to 36 nodes and 121 branches to accommodate zonation of the system. Nodes such as primary producers, herbivores, and

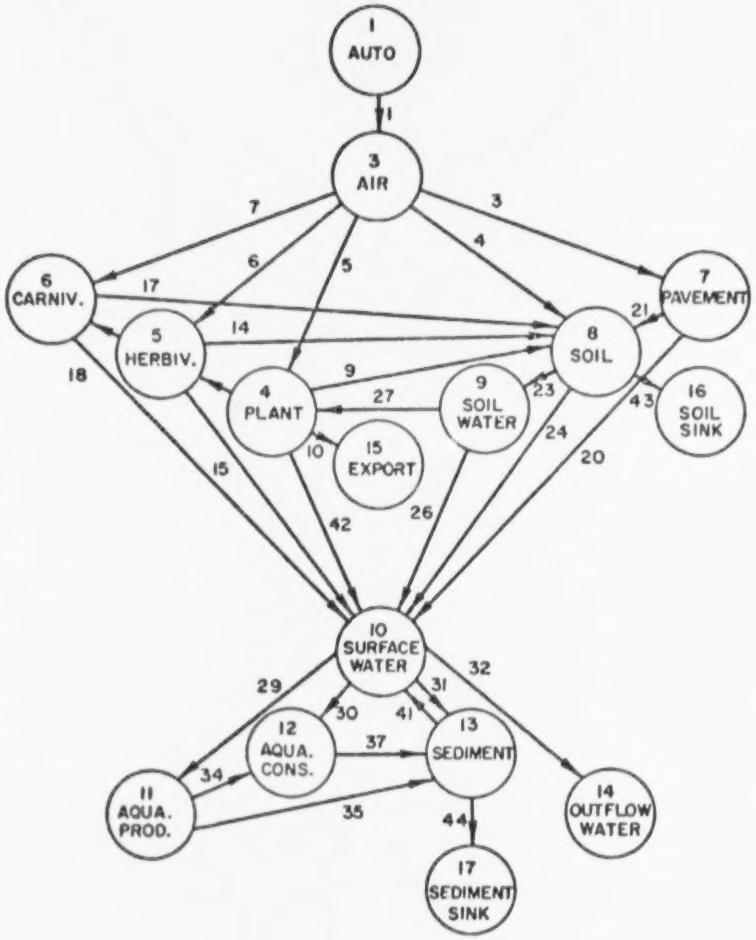
1
AUTO
1
3
AIR
7
3
6
5
4
6
CARNIV.
17
7
PAVEMENT
5
HERBIV.
14
21
8
SOIL
18
9
4
PLANT
27
9
SOIL
WATER
23
16
SOIL
SINK
43
10
15
EXPORT
24
20
15
42
26
10
SURFACE
WATER
29
32
31
30
41
12
AQUA.
CONS.
13
SEDIMENT
37
34
11
AQUA.
PROD.
35
44
14
OUTFLOW
WATER
17
SEDIMENT
SINK

Figure 8.3 A network representation of a lead ecosystem model. Adapted from Rolfe et al., (1972).

carnivores are defined generally in this preliminary model, but future refinement and data availability may permit more detailed examination of these compartments. The procedure to simulate the flow of lead through the network consists of four steps: (1) generation of a distribution factor for each branch; (2) seasonal adjustment of the distribution factors; (3) updating of the nodal accumulation by adding the external inflows; and (4) distribution of the lead in the nodes through exiting branches (including self-loops). A formula is developed which yields nodal lead content changes between time periods. A computer program which performs the distribution provides the user with nodal accumulations and concentrations, including averages, standard deviations, minima, and maxima. Plots of nodal accumulations or concentrations may also be obtained. Table 8.11 shows typical results of 100 cycle (2 years) simulation using a zoned network of 36 nodes and 121 branches. Additional refinements in the system should permit (1) the study and prediction of lead transport and accumulation in ecosystems, and (2) the development of alternatives of lead pollution control.

The environmental fate and effects of cadmium and lead were studied in a laboratory model ecosystem with a terrestrial/aquatic interface, using silica sand, Bloomfield soil (sandy loam) and Drummer soil (silty clay loam) as substrates (Lu, et al, 1975). Applications were made directly to the substrates as lead and cadmium chloride and as sewage sludge as a source of heavy metals. The mobilization and incorporation of cadmium and lead into food chain organisms were inversely proportional to sorption capacity of the substrate and were highest in silica sand and lowest in Drummer soil. Following the application of sewage sludge there was clear-cut mobilization and transfer of cadmium, copper, lead, and zinc into food chains, alga (Oedogonium cardiacum), daphnia (Daphnia magna), mosquito larva (Culex pipiens quinquefasciatus), snail (Physa), and fish (Gambusia affinis). Cadmium exerted a particularly adverse affect on the various organisms in the model ecosystem suggesting that its presence in relatively high levels in sewage sludge could become a limiting factor in its use on soils and for crop production.

8.3.3 Aquatic Ecosystems

Several completed and on-going studies have been reported on lead concentrations in aquatic ecosystems. Wolf and Rice (1972) have detailed the following major information needs for estimating mineral reservoirs in estuaries:

(1) Determining the relative amounts of different physio-chemical forms of an element or radioiosotope in natural waters, their relative stabities, and the ease of introconversion between the various forms.

(2) Determining the relative biological availabilities of these different physiochemical forms to various types of biota.

(3) Determining trophic structure of the entire ecosystem.
The role of microorganisms--as sources of metallic
elements to consumers in detritus-based food chains,
as producers of organic-metal complexes, and as remineralizers of metals previously incorporated into plant or animal tissues--is particularly poorly understood.

TABLE 8.11 COMPARISON OF ACTUAL WITH PREDICTED LEAD CONCENTRATIONS IN MODEL ECOSYSTEM

Node	Average Concentration in Zone, ppm							
	I		II		III		IV	
	Predicted	Actual[b]	Predicted	Actual[b]	Predicted	Actual[b]	Predicted	Actual[b]
Soil & soil sink	63	50	26	23	17	13	128	115
Plants & litter	5	35	0.78	18	0.03	5	41	38
Herbivores	5	12	0.7	5	0.04	4	16	-
Carnivores	3	12	0.4	9	0.02	4	10	-

[a] Source: Rolfe, et al. Reprinted, with permission from J. Environmental Systems, (c) Baywood Publishing Co.

[b] Actual concentrations are based on preliminary data.

(4) Determining feeding rates and assimilation efficiencies for carbon and metallic elements at each major trophic interaction.

(5) Determining biological retention of metallic elements in the major organisms consumed by man.

(6) Determining the interactions of variable environmental parameters on reservoir size and transfer rates at each step in the overall system.

As a minimum, this information is necessary for any type of ecosystem to determine the extent of mineral cycling. Although data exist on points one and two for several ecosystems, few studies explain the remaining points and no studies were found in which all points of information were determined for the same ecosystem.

Banus, et al., (1975) measured the amounts of lead, zinc, and cadmium in various components of a salt-marsh ecosystem that had been experimentally treated with two levels (8.4 and 25.2 grams per square meter) of metals-containing sludge fertilizers. Figure 8.4 summarizes the annual budget of lead at three treatment levels including a control. It was found that lead entering the salt marsh was largely retained by the surface sediments but 6 to 8 percent was taken up by marsh grasses. Lead in grass tops was exported as detritus to deeper waters but this loss was only about 3 to 4 percent of the entering lead. Nitrogen added in conjunction with the metals resulted in an increased movement of the metals into coastal waters due to increased production of grasses and increased metal contents of the grass tops.

Drifmeyer and Odum (1975) investigated disposal of heavy-metal-containing dredge spoil and its possible uptake by salt-marsh biota. Fine-grained dredge spoil had considerably higher levels of lead, zinc, and manganese than did natural salt-marsh sediment. Large differences in the metals content of the spoil were found; these were dependent on the sediment type. Lead levels in the grass shrimp (Palaemonetes pugio), mumichog (Fundulus heteroclitus), common reed (Phragmites communis), saltmarsh cordgrass (Spartina alterniflora), and saltmeadow hay (Spartina patens) were significantly higher (at the 0.01 confidence level) than in these same species from the natural saltmarsh (see Figure 8.5). Concentrations of lead and manganese tended to decrease markedly with increasing trophic levels in both detritus-based and grazing food chains of the dredge-spoil pond (see Figure 8.6). Combining information on lead levels obtained by Drifmeyer and Odum (1975) with that on the feeding behavior of the above species, Drifmeyer (1975) was able to: (1) verify that lead from polluted, dredged material does enter the food web; and (2) determine the probable pathways of lead transfer in the dredge-spoil pond ecosystem (see Figure 8.7).

It is evident from the research data that material dredged from polluted waterways may constitute a source of lead uptake by salt-marsh plants and animals. Lead from polluted dredge spoil enters and is transferred without biological magnification through a simple sediment-marsh grass-detritus-grass shrimp-mumichog food web.

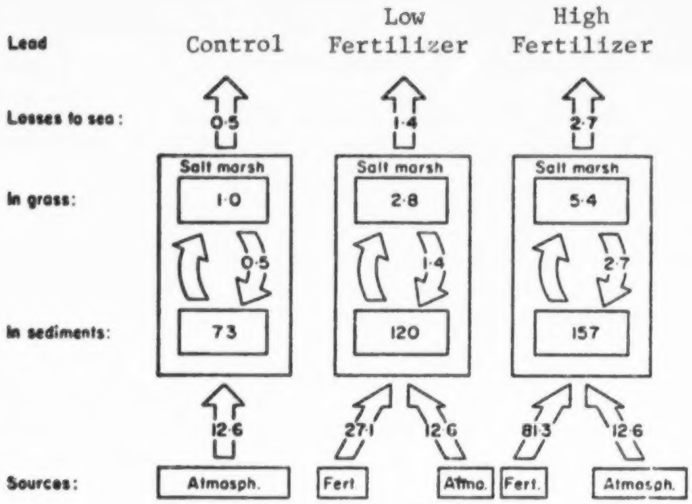
Lead
Control
Low Fertilizer
High Fertilizer
Losses to sea:
0·5
1·4
2·7
Salt marsh
Salt marsh
Salt marsh
In grass:
1·0
2·8
5·4
0·5
1·4
2·7
In sediments:
73
120
157
12·6
27·1
12·6
81·3
12·6
Sources:
Atmosph.
Fert
Atmo.
Fert.
Atmosph.

Figure 8.4 Calculated annual budget for lead in salt marsh plots under the three treatments. All values are in mg Pb m^{-2}. The boxes indicate pools while the arrows show annual fluxes. Source: Banus, et al. Reprinted with permission from Estuarine Coastal Marsh Science. (c) Academic Press Inc., (London) Ltd., 1975.

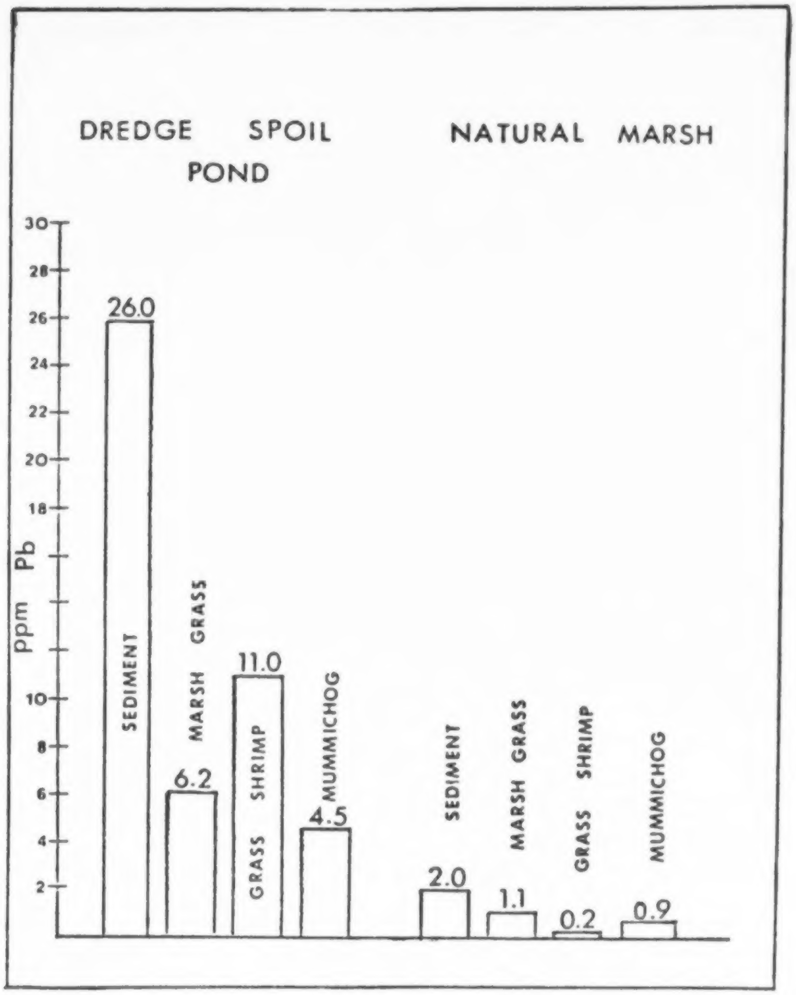

Figure 8.5 Lead levels in dredged material disposal sites of Craney Island and Lynnhaven inlet compared with that of the natural, unpolluted marsh at Mobjack Bay, Virginia. Source: Drifmeyer. Reprinted with permission from World Dredging and Marine Construction. (c) Symcon Publishing Corporation, 1975.

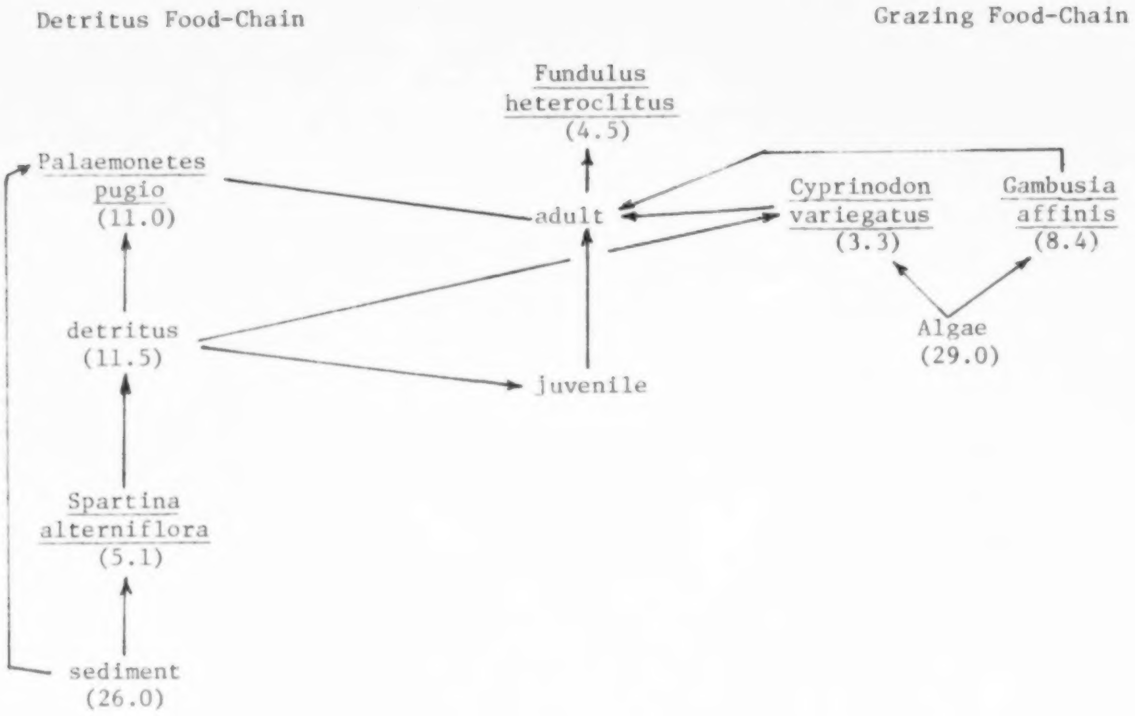
Detritus Food-Chain
Grazing Food-Chain
Fundulus heteroclitus (4.5)
Palaemonetes pugio (11.0)
adult
Cyprinodon variegatus (3.3)
Gambusia affinis (8.4)
detritus (11.5)
Algae (29.0)
juvenile
Spartina alterniflora (5.1)
sediment (26.0)

Figure 8.6. Pb transfer (ppm dry-weight) in a dredge-spoil pond ecosystem. Note the decrease in Pb levels with each successive trophic level in both simple food-chains. Arrows indicate trophic interactions.

Source: Drifmeyer and Odum. Reprinted, with permission, from Environmental Conservation. (c) Foundation for Environmental Conservation. (1975).

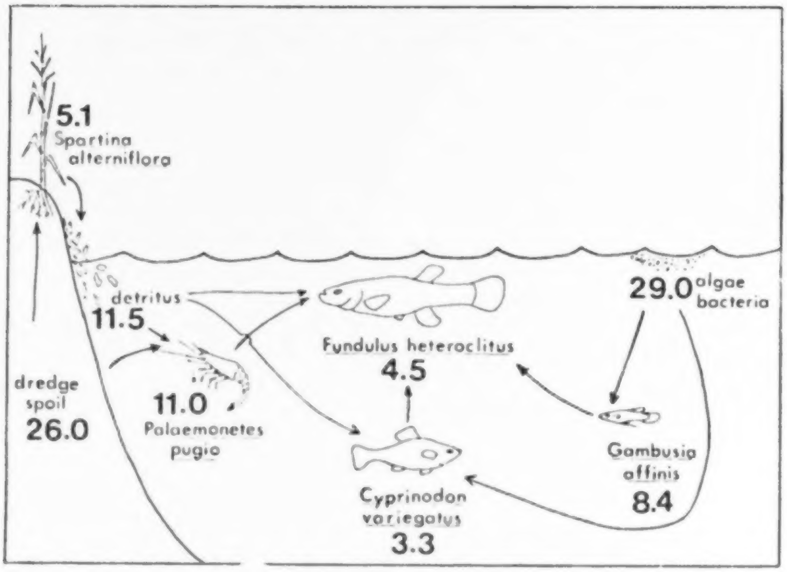
5.1
Spartina
alterniflora
detritus
11.5
29.0
algae
bacteria
Fundulus heteroclitus
4.5
dredge
spoil
26.0
11.0
Palaemonetes
pugio
Gambusia
affinis
8.4
Cyprinodon
variegatus
3.3

Figure 8.7 Average lead concentrations in dredge-spoil pond ecosystem, ppm dry wt. Arrows indicate probable pathways of lead transfer. Source: Drifmeyer. Reprinted with permission from World Dredging and Marine Construction. (c) Symcon Publishing Corporation, 1975.

Mechanistically, Bella and McCauley (1971, cited in Drifmeyer and Odum, 1975) observed that heavy metals may be adsorbed on particulate matter in estaurine water and these metal-laden particles may be pelletized by various animals and deposited in the estaury. Schubel (1972) noted that some filter-feeding and deposit-feeding organisms may be exposed to diets with relatively high concentrations of adsorbed heavy metals.

Gale, et al., (1973 and 1975) have investigated the various experimental factors and current industrial practices which may affect stream conditions in Missouri's New Lead Belt. These investigators have concluded that the most serious threat to aquatic life and environmental stability are (1) the release of gangue with varying amounts of residual metal ores, and (2) the release of toxic milling reagents into receiving streams. Aquatic vegetation and leaf litter material have been shown to bind large quantities of lead. Lead is bound to the anionic sites on the surface of aquatic plants or in leaf litter by ion exchange. Ion exchange capacities of mixed live algal cultures averaged approximately 65 milliequivalents of lead per 100 grams dry weight. Similar cation exchange capacities for leaf litter collected in the region of the smelter approximated 180 milliequivalents of lead per 100 grams dry weight. Biomagnification of lead was not found in the different aquatic organisms. Rather, the elevated total body concentrations of lead in fish, tadpoles, crayfish, and aquatic arthropods were associated with gastrointestinal contents with some additional lead bound or chelated to the mucous membranes of gills or to the mucous covering body surfaces. The investigators believe that under present operational conditions, lead toxicity will not become a problem to aquatic life forms in Missouri's New Lead Belt. However, further research is suggested to determine the cause of increased algal growth below the industrial outfalls, and particularly, the factors which permit the dominance of diatomaceous forms and the exclusion of normal consumer organisms in some of the problem streams.

Mathis and Cummings (1971) found that the lead content of sediments in the Illinois River was approximately 10,000 times greater than the water (see Figure 8.8). Mud samples taken from Lake Hamilton (Arkansas) and analyzed for trace elements (Nix, 1970) are shown in Table 8.12. The downstream enrichment (lower station numbers) of the bottom muds probably reflects the use of the reservoir.

Sediment in lakes and rivers represent a sink for lead in the ecosystem. However, it is still in the ecosystem and may be leached under appropriate conditions. Mathis and Cummings (1971) found that the content of lead in clams, worms and fish was much higher than that in the water. Worms contained lead in concentrations of the same magnitude as that found in the bottom sediments. The fish had considerably lower concentrations of lead; the carnivorous fish had slightly lower concentrations of lead than the noncarnivorous fish.

Schroeder and Balassa (1961) reported a range of 0.17 to 2.5 ppm of lead in seafood with an average of 0.5 ppm and only one sample exceeding 0.87 ppm. Harley (1970) reported a concentration of 0.31 ppm in shellfish. Pringle, et al., (1968) reported average wet-weight concentrations of 0.47, 0.70 and 0.52 ppm in Eastern oysters, soft-shell clams, and Northern quahogs, respectively. The ability of the Eastern oyster to concentrate lead was shown by

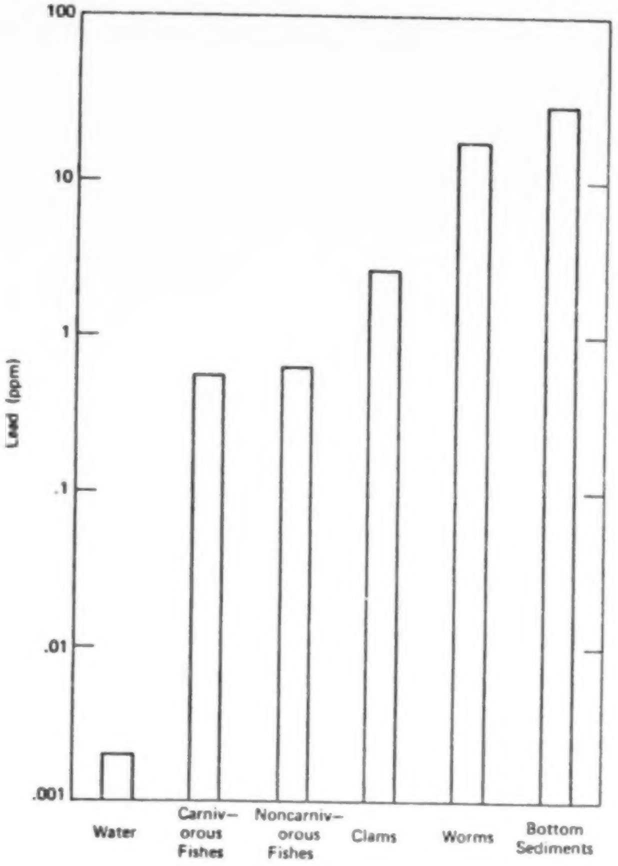

Figure 8.8 Mean concentration of lead in water, biota, and sediments of the Illinois River. Adapted from Mathis and Cummings (1971).

Table 8.12 LEAD CONCENTRATION IN MUD IN LAKE HAMILTON[a]

Station Number	Water Depth meters	Lead Concentration, μg/g
1	34	20
2	28	60
3	22	50
4	15	35
5	11	20
6	9	10
7	7	--
8	5	5

[a] Adapted from Nix (1970).

exposing oysters to flowing seawater containing lead concentrations of 0.025, 0.05, 0.1, 0.2 milligrams per liter. After 49 days, the total accumulations of lead amounted to 17, 35, 75, and 200 ppm (wet weight). The highest concentrations of lead in the oyster occurred in the digestive gland and the lowest concentration in the muscle tissue. Oysters exposed to the lower concentrations appeared normal. However, oysters exposed to the higher experimental lead concentrations showed considerably atrophy and diffusion of the gonadal tissue; edema; and a less distinct hepatopancreas and mantle edge.

The interference of lead with algal growth and development is described in Section 4.2.1.2. The concentration of lead by noncrop vascular plants in aquatic systems is described in Section 4.3.1.1. Translocation of lead in terms of soil-plant-water relations is discussed in Section 4.3.3. Variations in lead concentrations in certain fish tissues and evidence that elevated amounts of lead in fishes result from pollution are presented in Section 5.3.1.

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